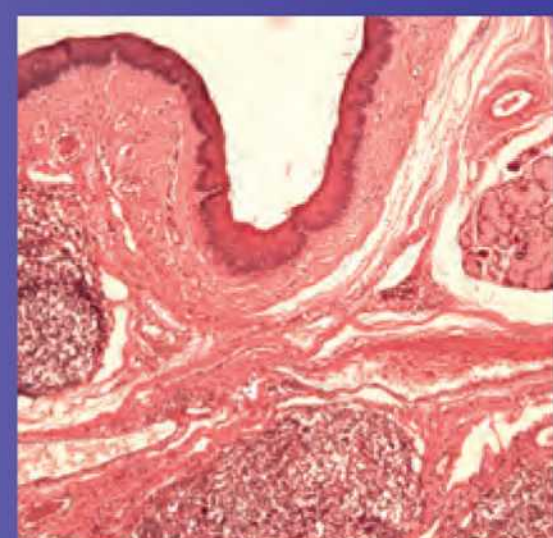
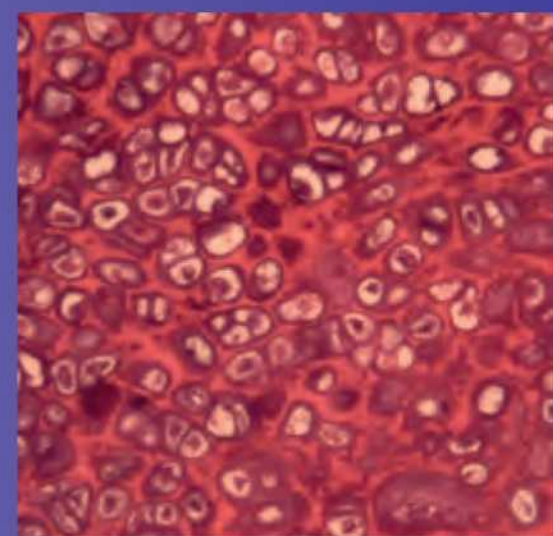
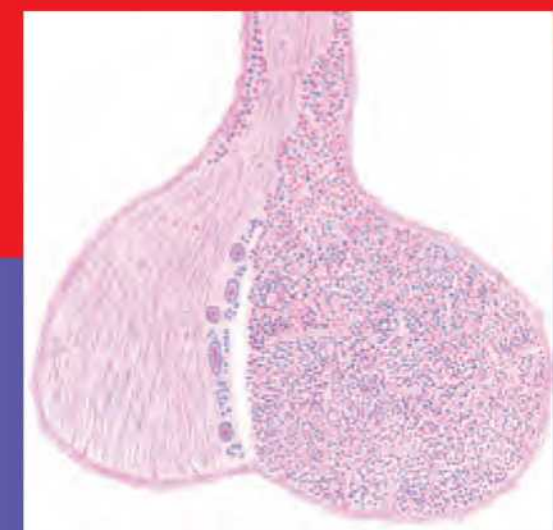
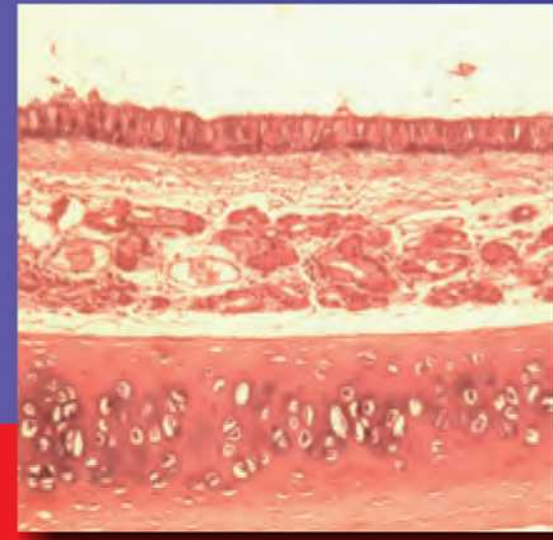


# HISTOLOGY

Text & Atlas

Brijesh Kumar

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# HISTOLOGY

**Text & Atlas**





# HISTOLOGY

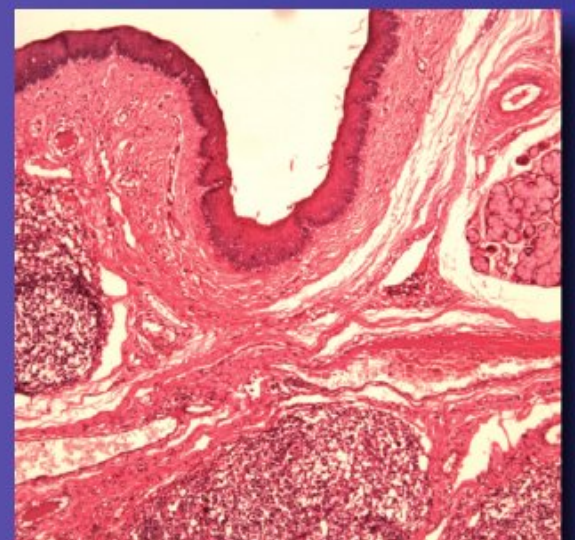
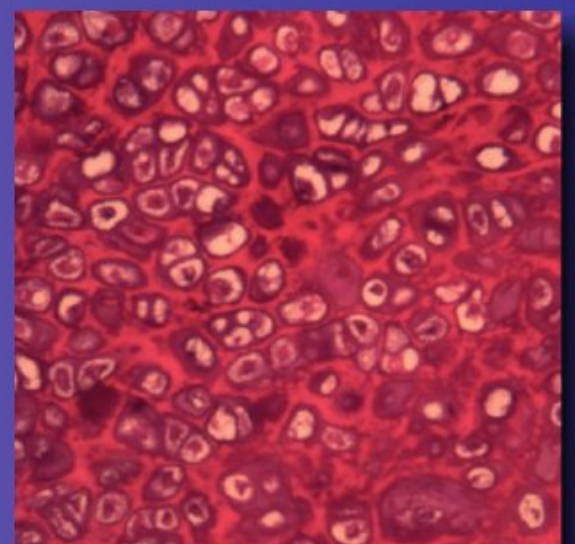
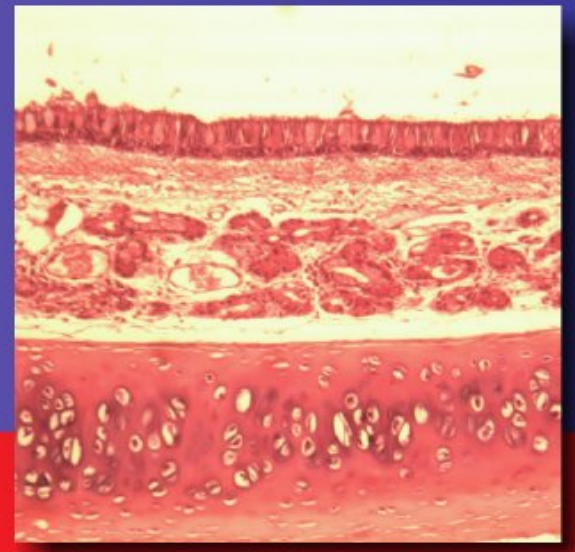
## Text & Atlas

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# Dedicated

To my late father, whose hard work and sacrifice enabled me to succeed in all that I have endeavoured

To my brother, who took over all the responsibilities after our father passed away

To my mother, for her unwavering support and profound devotion  
and

To my students, for always keeping me on my toes



# Preface

This book is a result of persistent feedback received from several of my students about the difficulties faced by them in understanding histology. The most common concerns related to understanding and replicating the diagrams correctly, differentiating between similar looking slides and getting a sound grasp of the conceptual details. It was to address these concerns that I took up the project of writing this book.

I have endeavoured to resolve the above-mentioned difficulties by presenting histology in a simple, interesting and lucid manner. I hope this will make it easier for students to understand and retain concepts as well as to reproduce the diagrams in their practical manuals.

The book caters primarily to the requirements of undergraduate medical and dental students. Pathology students will also find the book useful for refreshing histology fundamentals. Some of the key features of the book are as follows:

## The Diagrams

There are 118 coloured diagrams of histological slides. These simple, clear, well-labelled, hand-drawn diagrams will help the students in identification of the slides. They can be easily reproduced by them in the practical manuals. Important diagrams are also supported by relevant slides. The 186 line diagrams and three-dimensional illustrations given in the book will further aid understanding and retention.

## The Text

Based on the feedback given by an overwhelming majority of students, the text has been presented in a crisp, bulleted format. The information flows from basic to detailed with proper structuring in terms of headings and subheadings to enable easy comprehension.

## Identification of Similar Looking Slides

The book has 83 coloured photomicrographs (PMGs) of most of the organs. Studying these pictures will make the identification of actual histological slides easier for the students. Similar looking slides have been compared and their differentiating points have been enumerated separately in the text.

## Functional and Clinical Correlations

Several functional and clinical correlations have been mentioned. These not only make the topic interesting, but also help the students in understanding the importance of histology in the identification, diagnosis and pathogenesis of diseases.



## Key Points

At the end of each chapter, there are key points corresponding to the text and diagrams. These key points will enable a quick revision of the subject by the students.

It has taken me six years of hard work to bring forth this book to you. I hope that it will meet the expectations of my colleagues and requirements of the students. I shall welcome feedback for further improvement of the book.

Thank you for choosing to read this book.

**Brijesh Kumar**  
histology.by.brijesh@gmail.com

# Acknowledgements

I would like to gratefully acknowledge the many individuals without whom it would not have been possible to bring out the book in its present form.

I thank my brother, Rajesh Kumar, a constant constructive critic of mine, for teaching me the basics of computer usage, without which it would have been impossible to write this book electronically.

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I would also like to acknowledge my friends and colleagues, Dr. Sneha Guruprasad, Mr. Arvind Kumar Pandey, Mr. Alok Saxena, Dr. Tejodhar Pulakunta, Dr. Chakravarthy Marx, Ms. Suhani Sumalatha and Ms. Lydia S. Quadros for their support. Thank you, All!

Last but not least, I want to thank all my family members for their encouragement, especially my wife, Neeraj, and my son, Ishaan, who was born during the period I was working on this book and is 4 years old now. I often enjoyed being distracted by him during this journey.

**Brijesh Kumar**



# The Right Approach...

Very often, looking into a microscope does not interest the medical student aspiring to become a physician or surgeon. However, it is important to do this because a foundational knowledge of histology is vital for budding doctors, and these basics, if understood well, become interesting and even addictive!

## What is Histology?

Histology is the study of the microscopic anatomy of cells and tissues of humans, animals and plants. The term histology is derived by the combination of two Greek words, histos meaning 'tissue' and logia meaning 'the knowledge of'.

Histopathology is the microscopic study of diseased tissue.

## Why should it be studied?

Well, here are some of the reasons as to why you should study histology:

- **To understand the functions of an organ**  
The microscopic structure of an organ has a distinct correlation to its functioning and hence its histological examination helps in gaining a clear understanding of its functions.
- **For making pathological diagnosis**  
Histological examination of a diseased tissue is essential for diagnosing certain diseases. The diagnosis can be made by observing the digression in the histological appearance of the diseased tissue from the normal tissue. Hence, the importance of retaining histological understanding when studying pathology in the second year.

## How should it be studied?

The following points may be suggested for an effective comprehension of histology.

- **Concentrate on the building blocks**
  - The four basic tissues—epithelia, connective tissue, muscular tissue and nervous tissue—are the building blocks of all the organs of the body. Even though the arrangement of these tissues varies from organ to organ, it is consistent within an organ. The understanding of this concept is fundamental to the study of histology. So, study the four basic tissues thoroughly.
- **Analyse the histological slide before putting it under the microscope**
  - Look at the slide with the naked eye before putting in under the microscope. This will provide some clue as to what organ it could be.

- **Observe histological slides carefully under the microscope**
  - Notice the different types of basic tissues present in the histological slide.
  - Pay attention to the arrangement of the basic tissues and note how they have been modified in an organ.
  - Try to find the reason behind the presence of a particular basic tissue in the organ and its modification. This will not only help in identification of the slide, but it will also help in understanding the functions of an organ.
- **Know more to see more**
  - If you have understood the basics well and if you have read well, you will be able to observe more features in a histological slide than the student who has not read the topic in detail.
- **Don't cram**
  - Last but not the least, try to follow the above-mentioned method for systematically viewing and understanding a histological slide. If the understanding is sound, retention will happen. Don't focus on simply cramming for reproducing content in the exam.

**Brijesh Kumar**



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# Tissue Preparation for Histological Study

## STEPS OF TISSUE PREPARATION

To prepare tissue for histological slides, the following steps need to be taken:

### 1. Fixation

- The collected tissue sample is fixed to preserve tissue from degradation (autolysis and bacterial degradation) and to maintain the structure of the tissue.
- The most commonly used fixative is formalin.

### 2. Dehydration

- Removal of water from the tissue is necessary since water is not miscible with paraffin wax. Paraffin wax is used in embedding, which is described later.
- For removal of water, the tissue is submersed successively in alcohol solutions of increasing concentrations (70–100%).

### 3. Clearing

- Since alcohol is not miscible with paraffin wax, it has to be removed from the tissue; this is done by xylene.
- Xylene is miscible with paraffin wax.

### 4. Embedding

- The specimen is submersed into melted wax (the temperature of the wax should be just above its melting point).
- The wax replaces the clearing agent present inside the specimen.
- Now the tissue is allowed to cool, and as it cools the paraffin wax solidifies.
- The solid wax inside and outside the specimen provides physical support to the tissue, both internally and externally. This physical support is essential in obtaining very thin sections of the tissue.

### 5. Section cutting

- A small block of paraffin wax containing the tissue is prepared.
- Using the microtome (Fig. 1.1), around 5-µm-thick sections of wax-impregnated tissue are obtained.
- These wax-impregnated sections are floated on warm water (45°C); this allows the wax to fatten out.
- Now, the sections are mounted on glass slides (coated with adhesive) and stained.

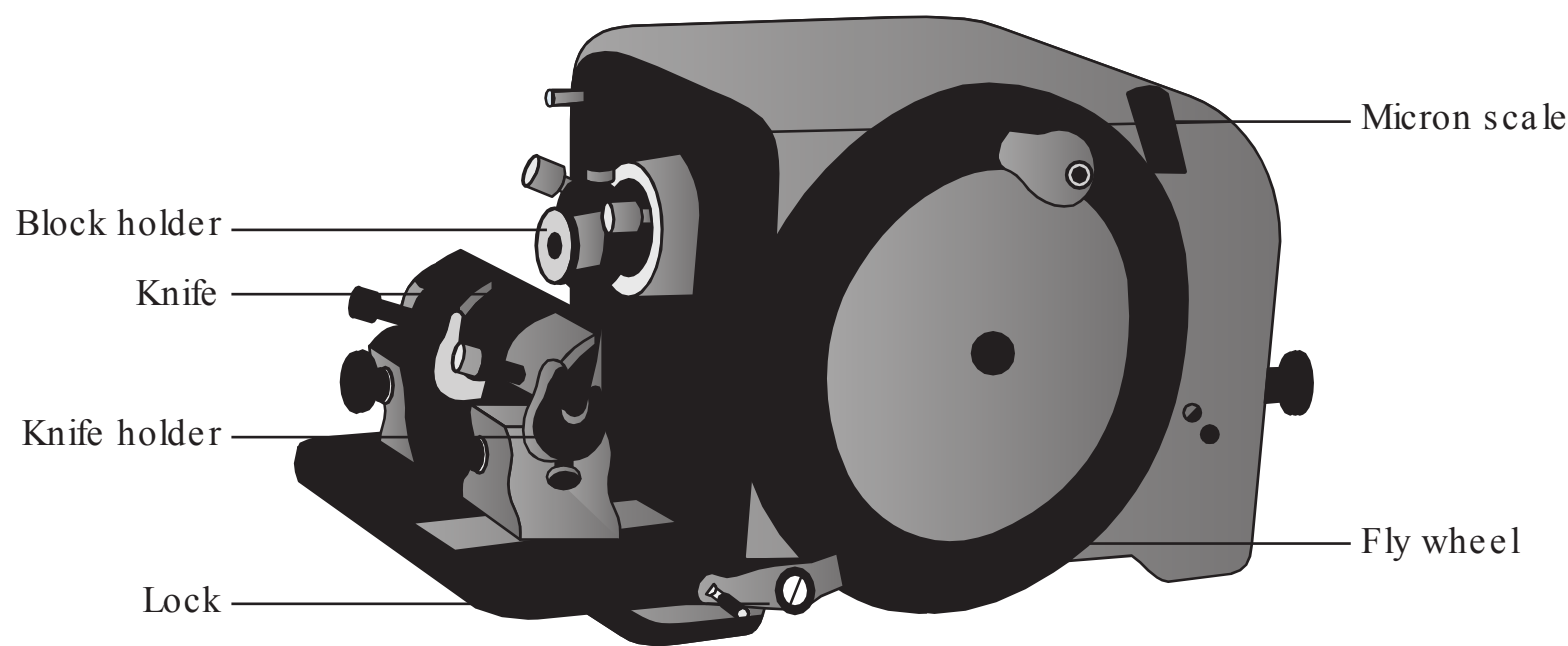
### 6. Staining

- Wax is removed from the section by xylene.
- The section is rehydrated and stained. Staining is essential as most of the tissues are colourless.
- Commonly used stains are discussed later in the chapter.

### 7. Mounting

- After the histological section is stained, a drop of mounting medium is added to the slide and a cover slip is placed on it. When the mounting medium solidifies, the cover slip gets adhered to the slide.
- Mounting medium commonly used is Canada balsam.





**Figure 1.1** Microtome. (Courtesy: Dr. D.R. Singh, Professor & Head, Department of Anatomy, Nepalgunj Medical College, Banke, Nepal.)

## STAINS

- The dyes used for staining are classified as acidic and basic dyes. Acidic dyes stain basic components of a cell, whereas basic dyes stain acidic components of a cell. Some of the acidic and basic dyes are mentioned in Table 1.1.
- Most commonly used dyes are haematoxylin and eosin (H&E).

**Table 1.1** Commonly Used Dyes

Acidic dyes	Basic dyes
Eosin	Haematoxylin
Acid fuchsin	Toluidine blue
Orange G	Methylene blue

### HAEMATOXYLIN (H)

- It is a basic dye.
- The cell components that stain well with haematoxylin are called basophilic. They appear purple.
- It stains nuclei due to an affinity to nucleic acids.

### EOSIN (E)

- It is an acidic dye.
- The cell components that stain well with eosin are called eosinophilic or acidophilic. They appear pink.
- It stains cytoplasm, mitochondria and collagen.

### OTHER STAINS

- Apart from the above-mentioned stains, there are stains which are used to stain certain specific components:
  - (a) Periodic acid–Schiff: It selectively stains carbohydrate-containing substances such as glycogen and basement membrane deep red.
  - (b) Sudan Black B: It specifically stains fat.
  - (c) Elastic Van Gieson stain: It stains elastic fibres black and collagen fibres red.

## SPECIAL HISTOLOGICAL TECHNIQUES

Although H&E stains are commonly used, special methods such as histochemistry, cytochemistry and immunochemistry are useful in diagnosing certain diseases and in biomedical research.

## HISTOCHEMISTRY AND CYTOCHEMISTRY

These methods are used for identifying and localising certain macromolecules in the tissue section. Enzyme activity and specific chemical reactions of macromolecules are the basis for their detection.

## IMMUNOCYTOCHEMISTRY

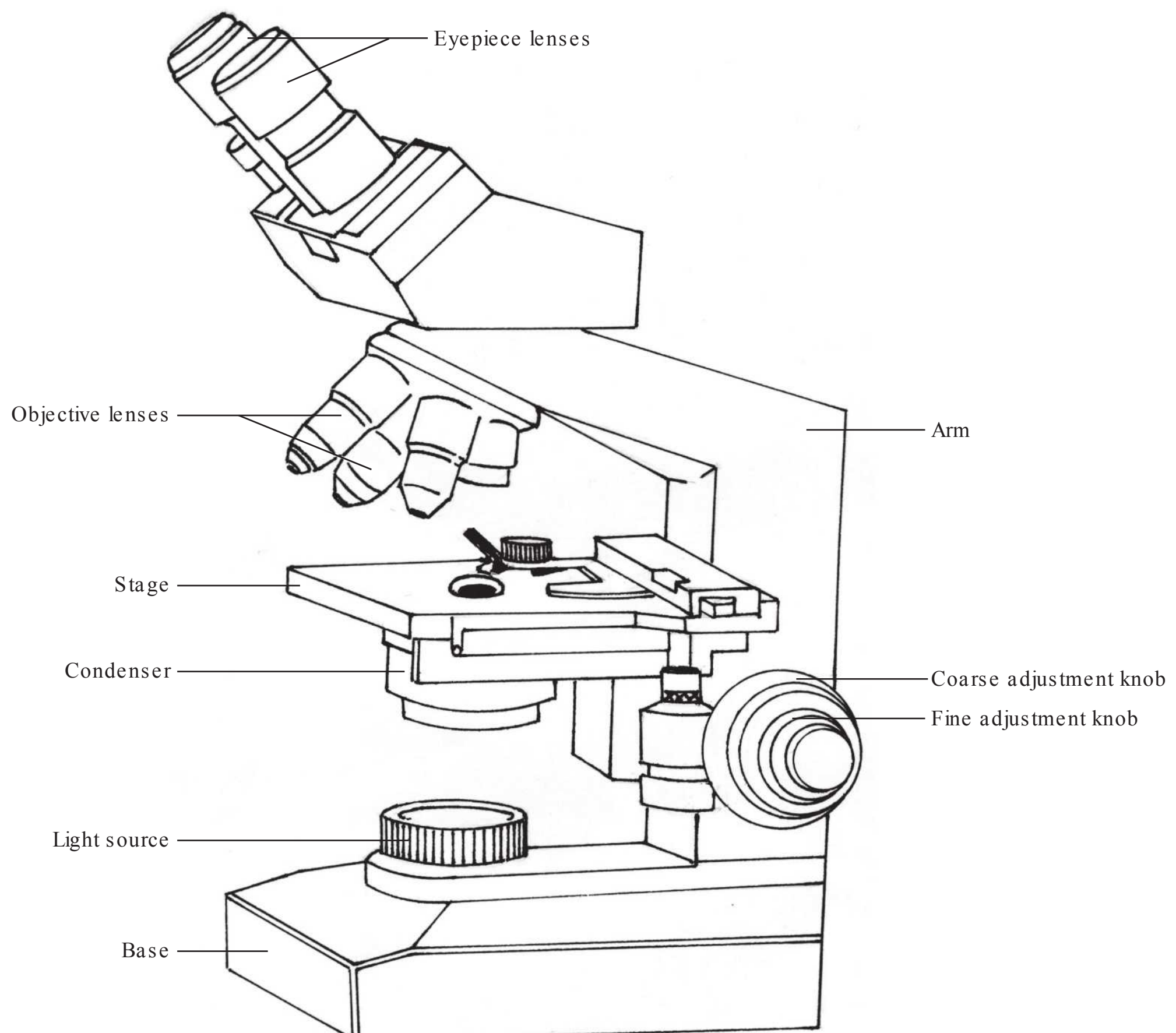
In this method, a specific protein (antigen) is detected by using the antibody against that specific protein. The antibodies used are tagged with a fluorescent molecule which helps in detection of antigen–antibody complex.

## LIGHT MICROSCOPE

The light microscope is so called because it employs visible light to detect small objects.

### PARTS OF LIGHT MICROSCOPE (Fig. 1.2)

- Eyepiece lens: It is the lens at the top that one looks through, and it brings the image into focus for the eye.

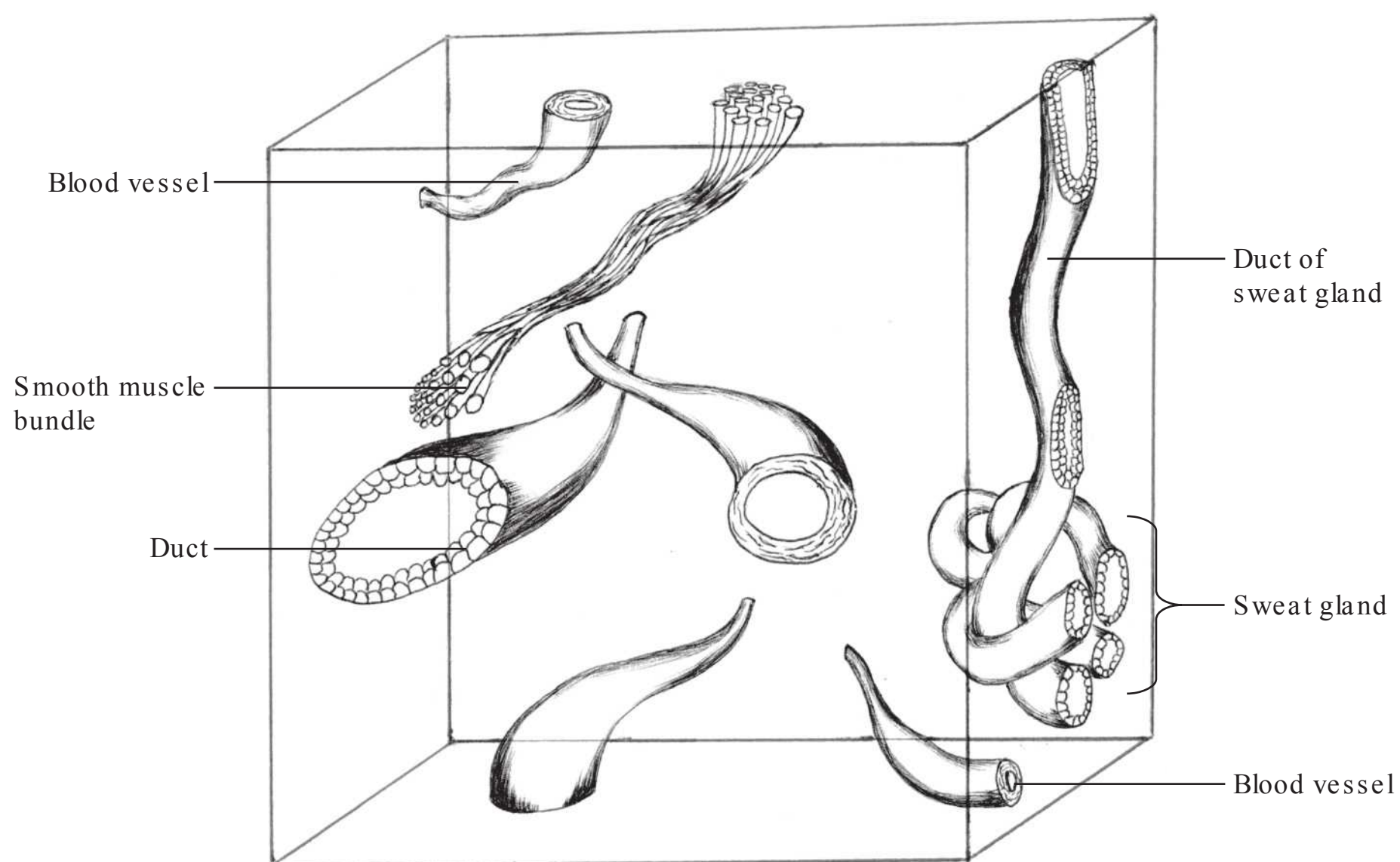


**Figure 1.2** Light microscope and its parts.

- Objective lens: It projects an enlarged and illuminated image of the object to the eyepiece. Usually, there are three or four objective lenses in a microscope. Most of the microscopes have objective lenses of 4X, 10X, 40X and 100X powers; 10X and 40X lenses are mostly used.
- Condenser: The function of the condenser lens is to focus the light onto the specimen.
- Support and alignment: This is provided by the arm, base and stage.
  - (a) Arm: It is a curved portion that holds all the optical parts.
  - (b) Base: It supports the weight of all the parts of the microscope.
  - (c) Stage: It is a platform on which the glass slide is placed.
- Light source: Better microscopes have a built-in light source. Natural light can be used as the light source in microscopes provided with a mirror (concave).
- Focusing knobs: When these knobs are rotated, they move the stage up and down for coarse and fine adjustment.

# Getting Oriented to the Sectional Planes

- The various structures (e.g. blood vessels, glands, nerve fibres and muscles) in the tissue sample from which the histological slide is to be prepared are organised in three-dimensional planes (Fig. 2.1).
- During the sectioning of the tissue, very thin slices of the tissue are made. These slices are two dimensional, which means they have only two planes.
- The various structures present in the tissue, which were organised in three dimensions in the intact tissue, also get cut into thin slices. As a result, in the slide we see these structures in two planes. Hence, the structures may appear totally different in the section from how they are in the intact tissue.



**Figure 2.1** Three-dimensional view of a tissue showing orientation of various structures present in it.

## INTERPRETING HISTOLOGICAL SLIDES

- While interpreting a histological slide, the observer needs to imagine the missing part of the structure which he/she is observing.
- As mentioned earlier, structures may appear different in different planes of the sections. Let us try to understand this with some examples.

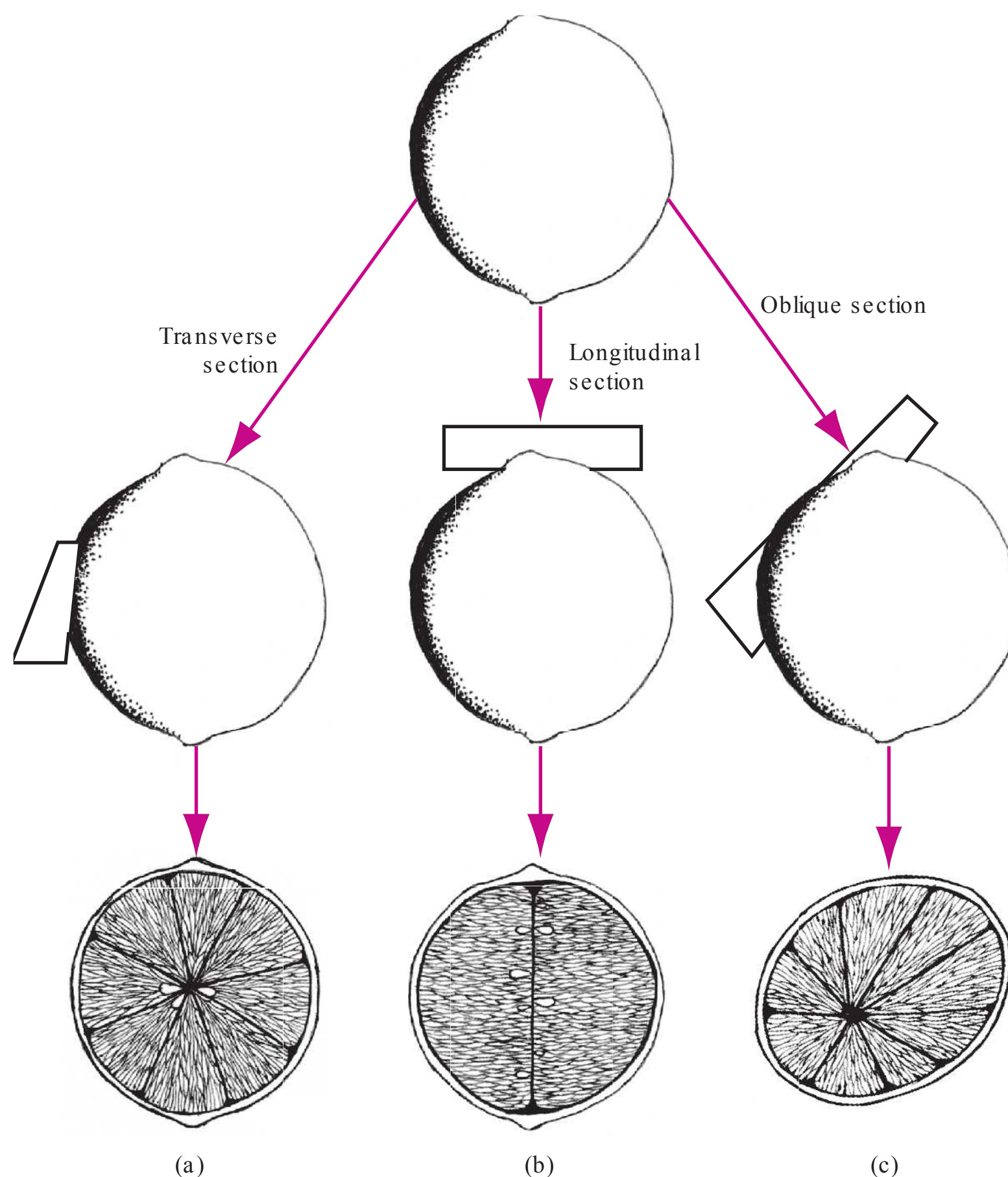


## SLIDE OF A SOLID STRUCTURE

For the purpose of easy understanding, a solid organ in the body can be compared to a lemon. The lemon can be cut in different planes and the changes in its appearance in those planes can be appreciated.

### Example: Sections of a Lemon

- A lemon is cut in transverse, longitudinal and oblique planes. Notice the change in the appearance in different planes (Fig. 2.2).
- Similarly, a solid structure in the tissue may appear different in different sectional planes in the histological slide.



**Figure 2.2** Appearance of a lemon as it is cut in (a) transverse, (b) longitudinal and (c) oblique planes.

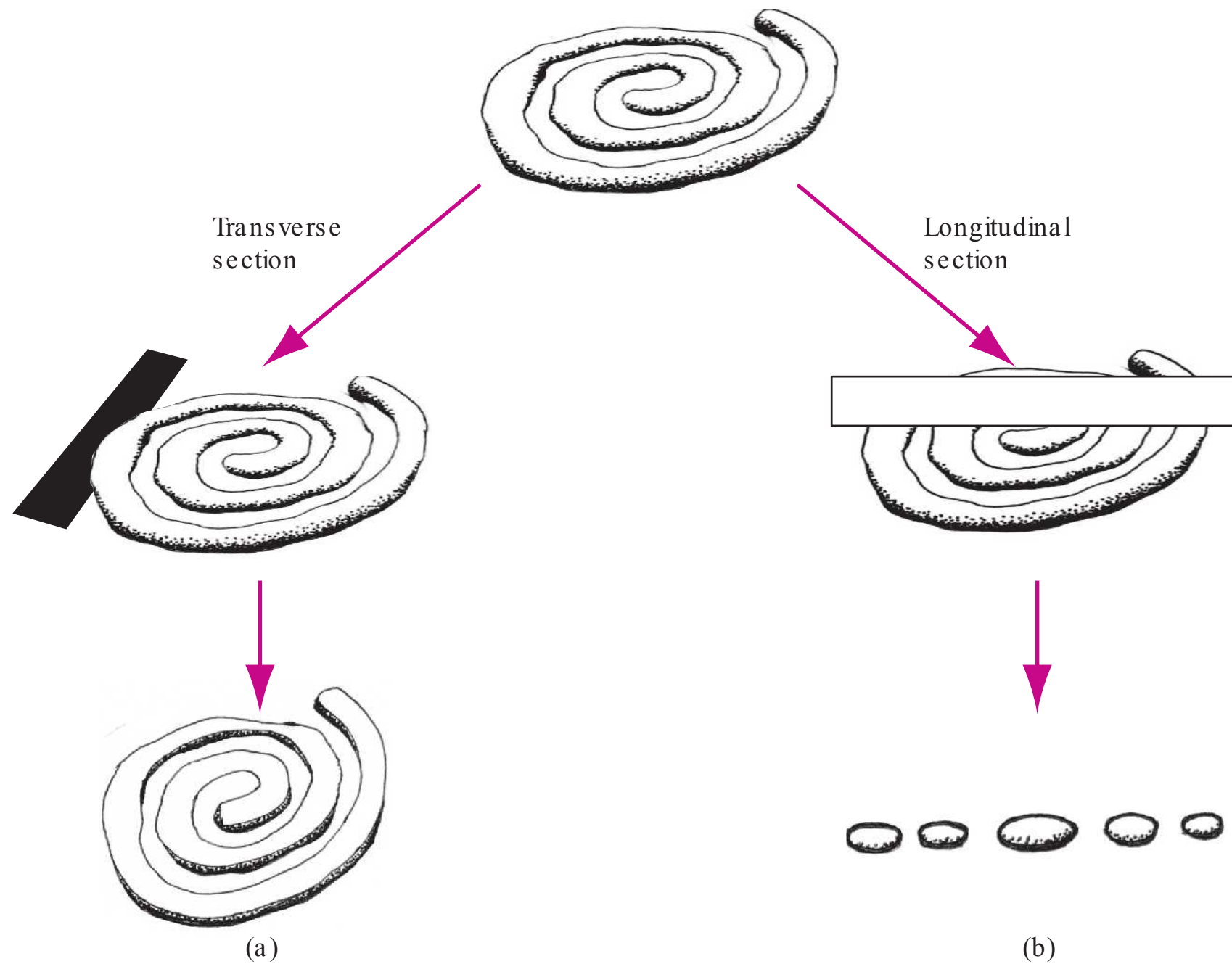
## SLIDE OF A TUBULAR STRUCTURE

For the purpose of easy understanding, a tubular structure in the body such as a blood vessel can be compared with a jalebi (the sweet).

### Example: Sections of a Jalebi (the Sweet)

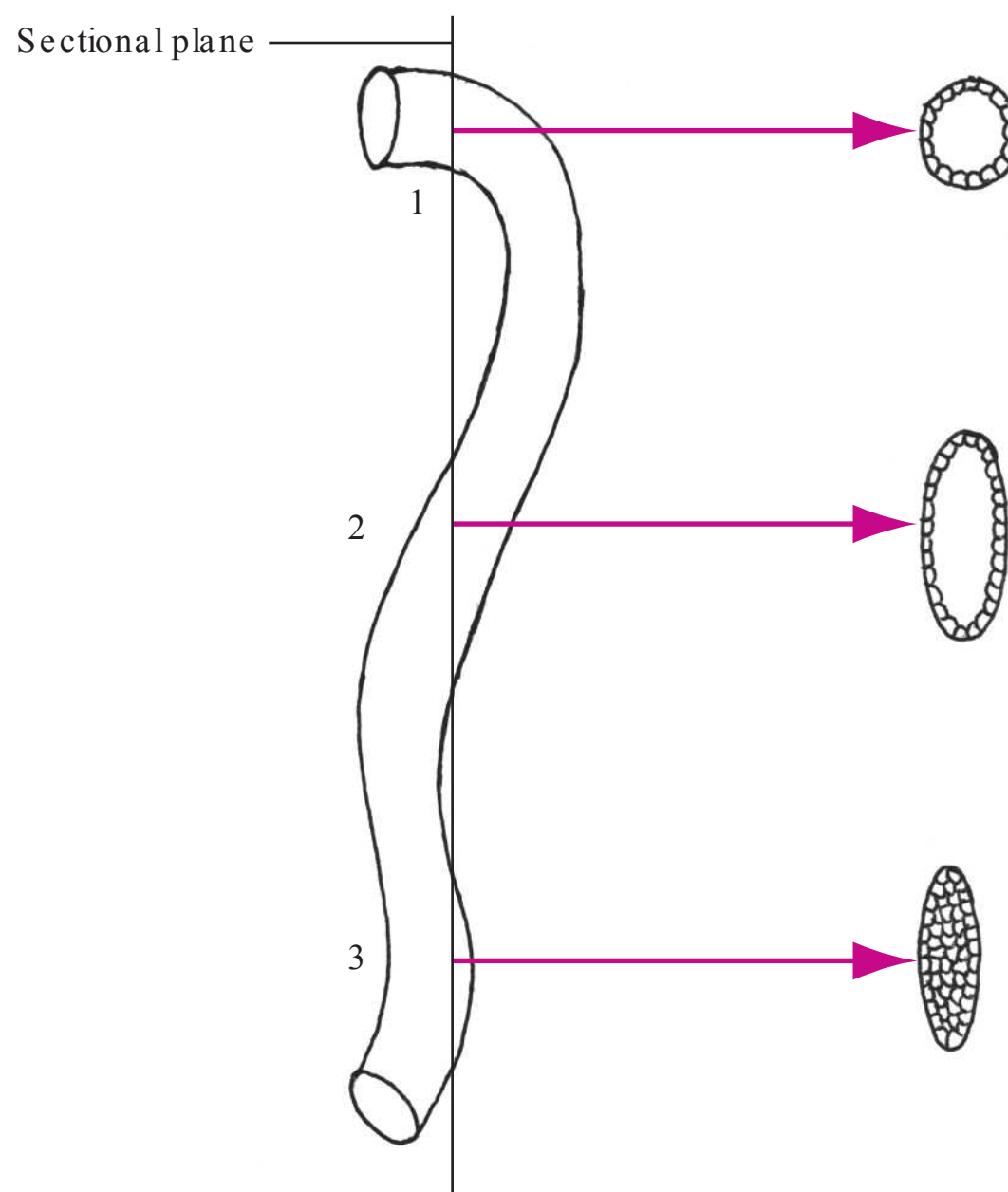
- A jalebi is cut in transverse and longitudinal planes. Notice how the appearance of a jalebi is totally different in the longitudinal section (Fig. 2.3).





**Figure 2.3** Appearance of a jalebi as it is cut in (a) transverse and (b) longitudinal planes.

- Similarly, in a tissue, the duct, blood vessel or any other coiled tubular structure will appear different in different sectional planes (Figs 2.1 and 2.4).



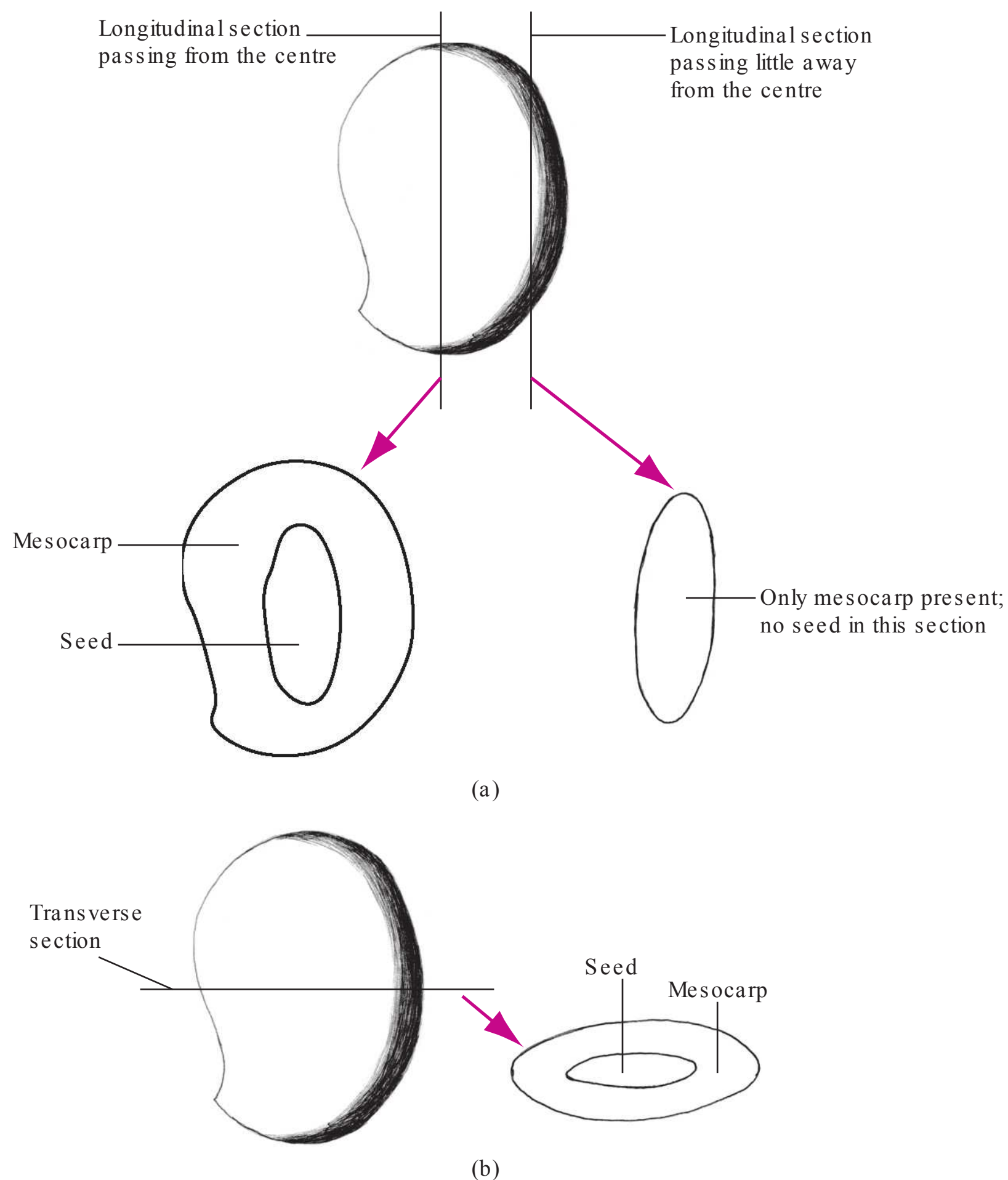
**Figure 2.4** A sectional plane that passes through a duct at three points: at point 1, the duct is cut transversely; at point 2, obliquely; and at point 3, longitudinally. Note that at point 3, the section passes through the wall of the duct, and hence in the section lumen is not seen.

## INTERPRETING A CELL IN HISTOLOGICAL SLIDES

For the purpose of easy understanding, a cell can be compared to a mango.

### Example: Sections of a Mango

- If the longitudinal section of a mango is taken in the centre, we can see the seed in the centre surrounded by the mesocarp (the part which is eaten) (Fig. 2.5).
- If the longitudinal section is taken at a little distance away from the centre so that the seed does not come in the sectional plane, the section will have only the mesocarp (Fig. 2.5). Similarly, in a histological slide, if the section does not pass through the nucleus of a cell, the cell will appear without a nucleus.
- While observing the histological slide, the plasma membrane may not be visible—notice the shape and arrangement of the nuclei.
- The shape of a nucleus will give the clue for the shape of a cell.
- The number of rows of the nuclei gives the information about the number of layers of the cells.



**Figure 2.5** Appearance of a mango as it is cut in (a) longitudinal and (b) transverse planes.

# The Cell

Cells are the structural and functional units of all tissues.

## TYPES OF CELLS

There are two types of cells: prokaryotic and eukaryotic cells.

### PROKARYOTIC CELLS

- They are single-celled organisms that lack a membrane-bound nucleus and membrane-bound cell organelles.
- Example: Bacteria.

### EUKARYOTIC CELLS

- Eukaryotic cells have two important features that prokaryotic cells lack: a nucleus and cell organelles with membranes around them.
- All eukaryotic cells consist of cytoplasm and cell organelles, bounded by plasma membrane.

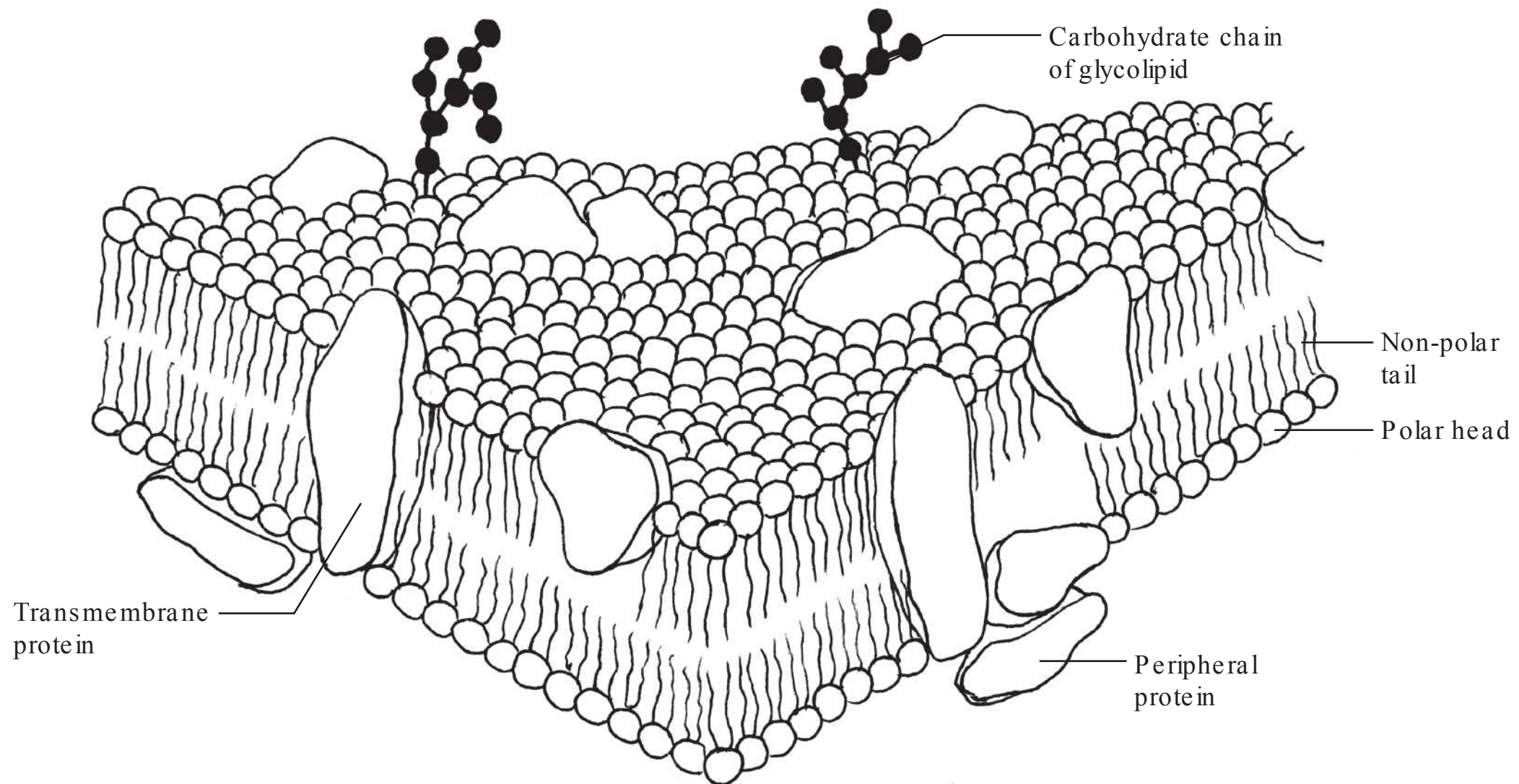
## PLASMA MEMBRANE

- Plasma membrane is also called plasmalemma.
- It separates the interior of cells from the external environment.
- The structure of a plasma membrane can be explained by the fluid mosaic model.

### FLUID MOSAIC MODEL

- The basic structure of plasma membrane and the membranes around the cell organelles is the lipid bilayer in which proteins and carbohydrates are interspersed.
- The fluid part refers to lipids of a cell membrane, and the mosaic part refers to proteins embedded in the lipid bilayer.
- Plasma membrane is not rigid, and the protein molecules can move sideways.
- There are three types of lipids in the plasma membrane: phospholipids, cholesterol and glycolipids; phospholipids are the most abundant (Fig. 3.1).





**Figure 3.1** Plasma membrane.

### Phospholipids

- Each molecule has a hydrophilic (polar) head and two hydrophobic (non-polar) tails.
- In the lipid bilayer, the tails project towards one another in the interior of the membrane and the polar heads are towards the surfaces of the membrane (Fig. 3.1).

### Proteins

- Membrane proteins are of two types: integral membrane proteins and peripheral membrane proteins.
- Membrane proteins that span the partial or entire thickness of the phospholipid bilayer are the integral membrane proteins. Integral membrane proteins that span the entire thickness of the lipid bilayer, with some parts that are exposed on both surfaces of the membrane, are known as transmembrane proteins.
- Membrane proteins which are located on the surface of the membrane are the peripheral membrane proteins. These proteins are exposed to the extracellular space.
- Membrane proteins allow the movement of substances into or out of the cells. They also act as receptors and enzymes.

### Carbohydrate

- Plasma membranes also contain carbohydrates, predominantly glycoproteins and glycolipids.
- They are present on the outer surface of the plasma membrane.
- They enable cells to attach to other cells or to extracellular matrix components. They also help in binding antigens and enzymes to the surface of the cell.

## FUNCTIONS OF PLASMA MEMBRANE

The plasma membrane performs a number of functions, which are as follows:

1. **Forms a barrier which is selectively permeable:** The plasma membrane acts as a barrier between the interior of a cell and its external environment. However, this barrier is permeable for certain substances and it regulates the entry and exit of these substances. The process by which molecules move across the plasma membrane is described under the section ‘Transport Across the Cell Membrane’.

**2. Aids in cell-to-cell communication:** Intercellular interaction is essential for proper functioning of multicellular organisms. Cells secrete chemical messengers which bind to the protein receptors on the plasma membrane of the target cells.

### TRANSPORT ACROSS THE CELL MEMBRANE

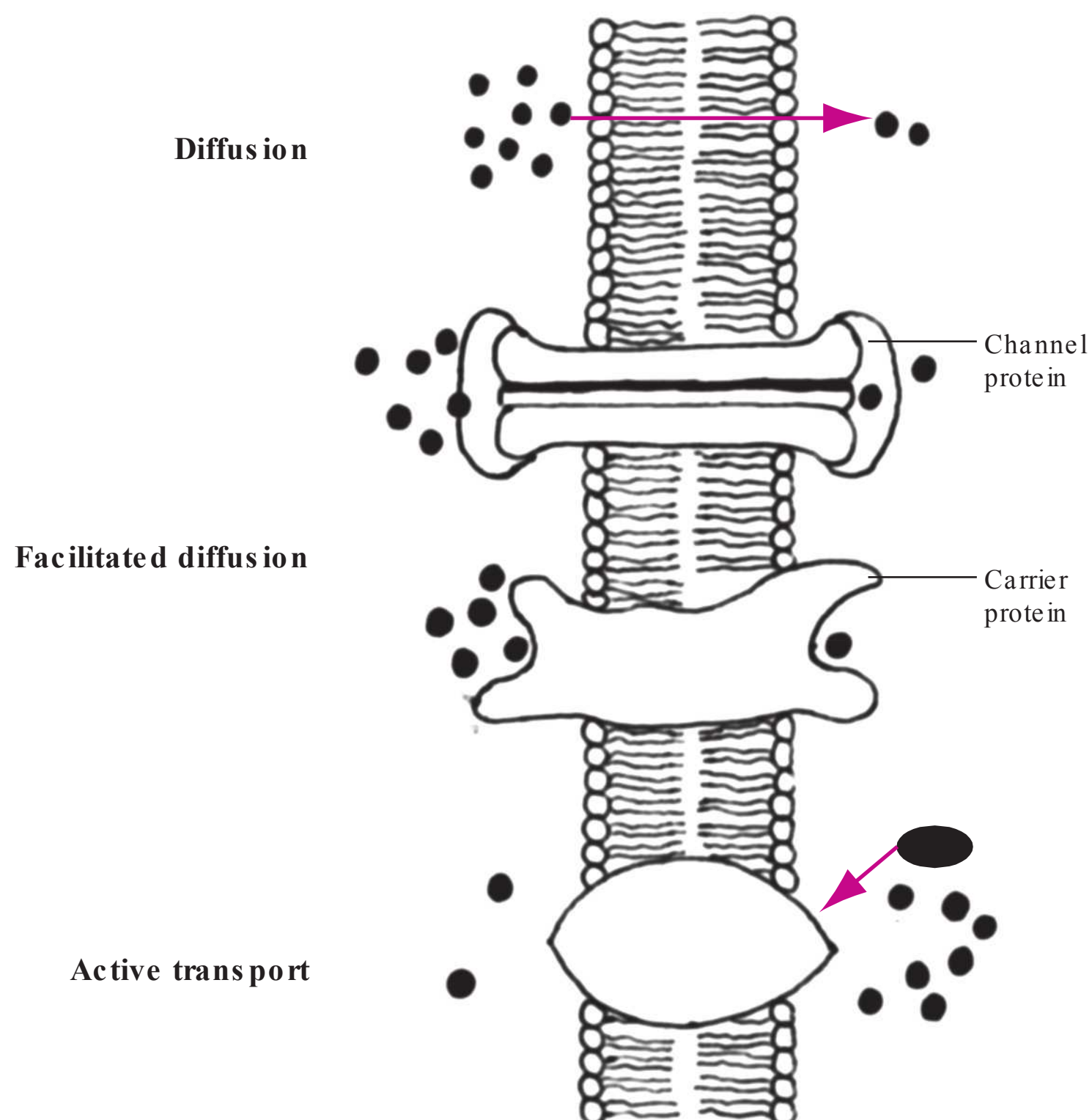
Substances can be transported across the plasma membrane by passive and active transports. They can also be transported across by vesicular transport; in this process membrane-bound vesicles (containing the substances to be transported) are formed in the cytoplasm.

#### Passive Transport

- In passive transport, substances can pass through the plasma membrane passively; the process does not require energy.
- Passive transport includes simple and facilitated diffusion.
- Diffusion is a process by which molecules or ions move from the region of higher concentration to the region of lower concentration, that is down their concentration gradient. Cations move to negatively charged regions and anions to positively charged regions, that is down their electrical gradient.

#### *Simple Diffusion* (Fig. 3.2)

- Molecules that are transported through simple diffusion are water, oxygen, carbon dioxide, glycerol, etc.
- The rate of diffusion is slow.



**Figure 3.2** Transport across the cell membrane.



**Facilitated Diffusion** (Fig. 3.2)

- Certain molecules require channel or carrier proteins to move across the plasma membrane. This is facilitated diffusion. As mentioned earlier, this process does not require energy.
- The substances which are transported through this process are urea, glucose, ions, etc.
- Channel proteins are transmembrane proteins, through which certain small water-soluble molecules pass.
- Carrier proteins are also transmembrane proteins. These proteins undergo reversible conformational changes to move the molecules from one side of cell membrane to the other. Carrier proteins are highly specific for the molecules to be transported. They are involved in passive as well as active transport.

**Active Transport** (Fig. 3.2)

- Cells need to transport some substances through plasma membrane against the concentration or electrical gradient. Also, certain substances cannot diffuse through the cell membrane. Transport of such substances is done by active transport.
- This process requires energy which is provided by ATP.
- Proteins involved in active transport are referred to as pumps. One such pump is the sodium–potassium pump.

**Vesicular Transport**

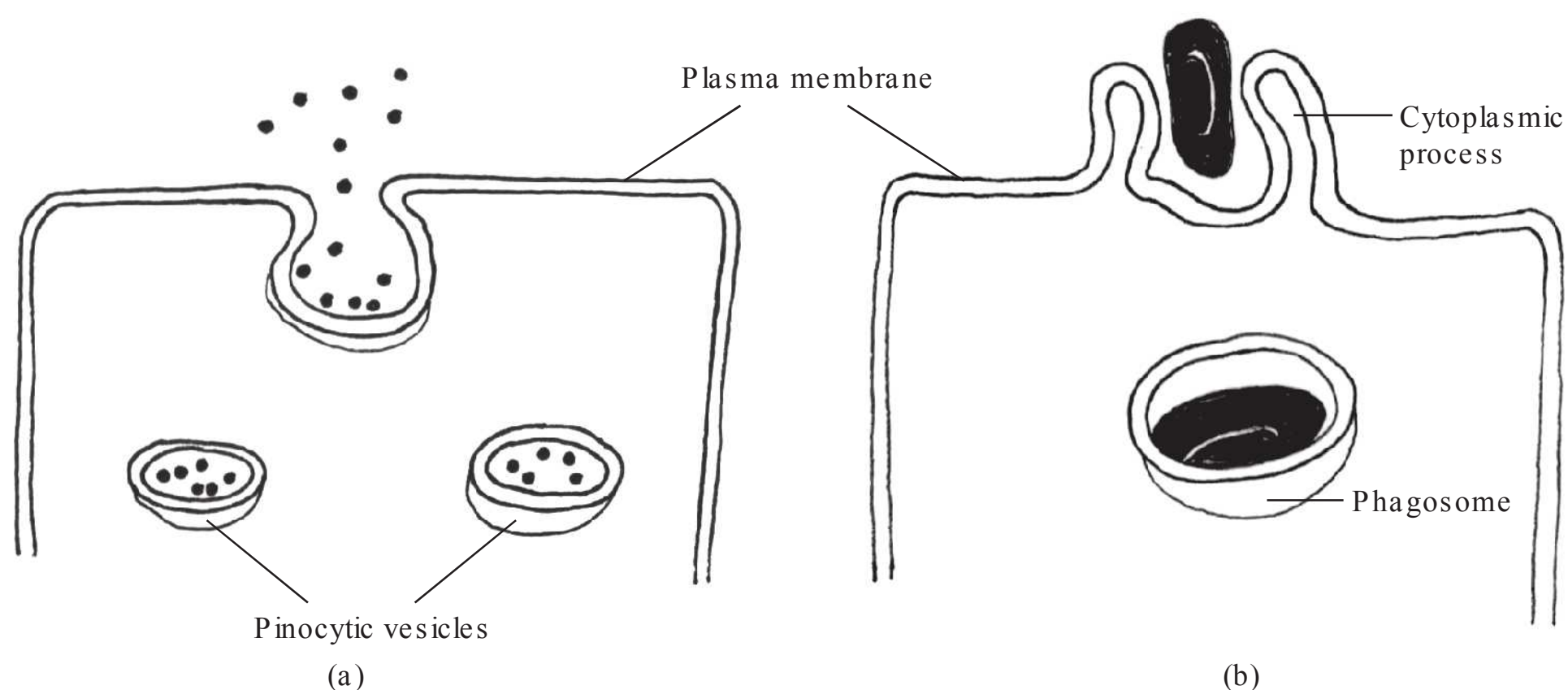
- Large molecules such as polysaccharides or proteins cannot be transported by carrier proteins. Such substances are transported by the process known as vesicular transport.
- Vesicular transport involves formation of vesicles.
- It involves two processes: endocytosis and exocytosis.

**Endocytosis**

In this process, the extracellular material is brought inside the cell as membrane-bound vesicles. A part of the cell membrane is pinched off in the formation of vesicles and the extracellular material is engulfed inside the cell. There are three endocytosis processes: pinocytosis, phagocytosis and receptor-mediated endocytosis.

**1. Pinocytosis (cell drinking)**

- It is the process by which cells ingest small amount of extracellular liquid and small pinocytic vesicles are formed (Fig. 3.3a).



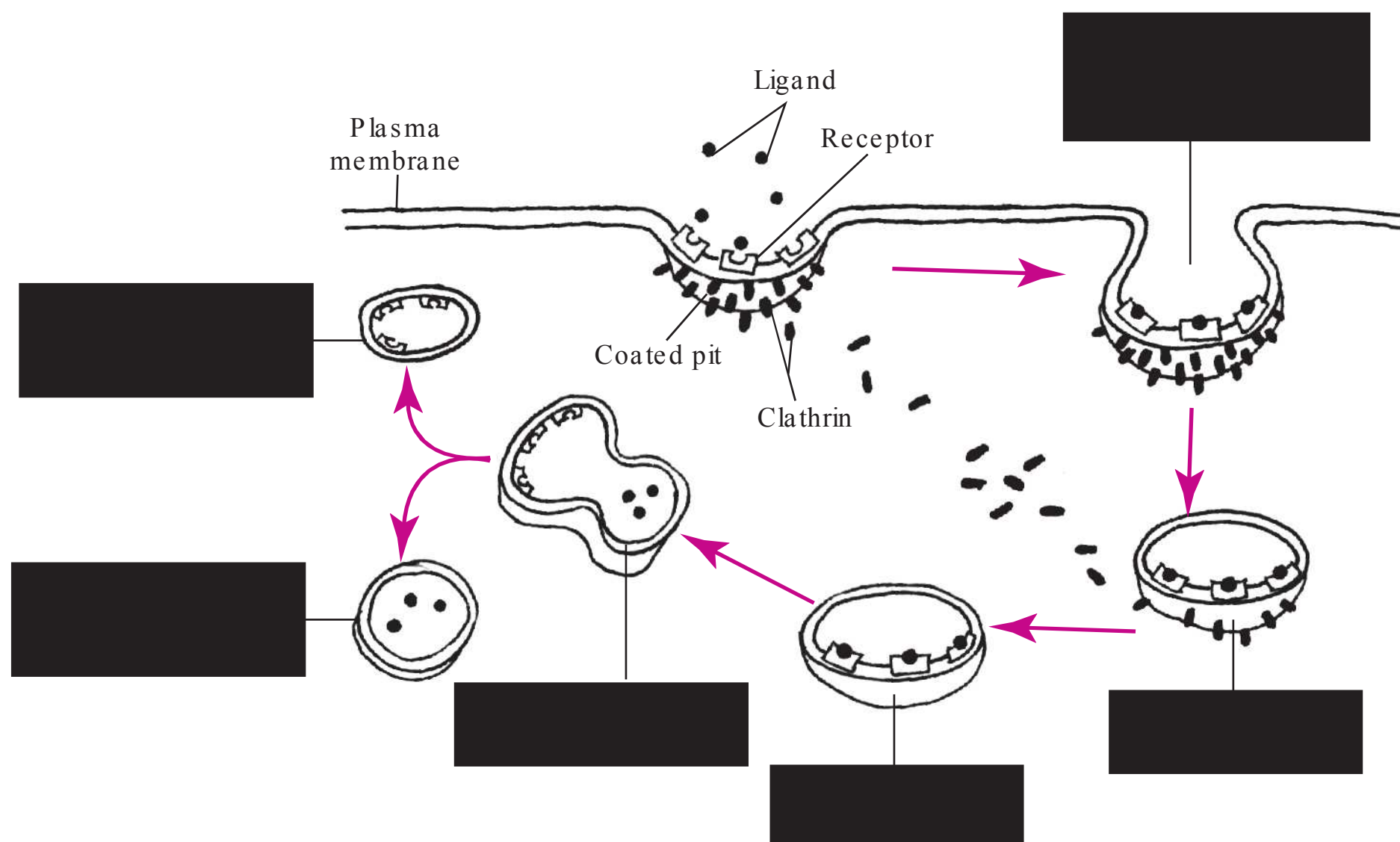
**Figure 3.3** (a) Pinocytosis and (b) phagocytosis.

## 2. Phagocytosis (cell eating)

- Cells ingest large substances such as bacteria, parasites and dead host cells through phagocytosis.
- The phagocytic cell extends cytoplasmic processes around the substance which is to be phagocytosed and ultimately surrounds it.
- Large-sized vesicles known as phagosomes are formed (Fig. 3.3b).
- Macrophages and neutrophils are the main phagocytic cells.

## 3. Receptor-mediated endocytosis (Fig. 3.4)

- Only specific substances such as peptide hormones are ingested by this process. These substances are known as ligands.
- Receptors for a specific ligand are present on the plasma membrane of the cell.
- Binding of the ligand to the receptor induces the receptors to accumulate at one location; these locations are known as coated pits (Fig. 3.4, step 1).
- Coated pits are small depressions in the cell membrane; the cytoplasmic surface of these pits has a protein (clathrin) coat.
- Coated pits invaginate and pinch off to form coated vesicles containing ligand–receptor complex (Fig. 3.4, step 2).
- Coated vesicles lose the clathrin coat (Fig. 3.4, step 3); clathrin which separates from the coated vesicles is reused in formation of new coated pits.
- The vesicle now fuses with the endosomes (not shown in Fig. 3.4). Endosomes consist of tubules and vesicles, and they are located near the plasma membrane. The acidic contents of the endosomes separate the receptors and ligands (Fig. 3.4, step 4). The receptors are reused (Fig. 3.4, step 5), whereas the ligands are transferred to lysosomes for digestion (Fig. 3.4, step 6).



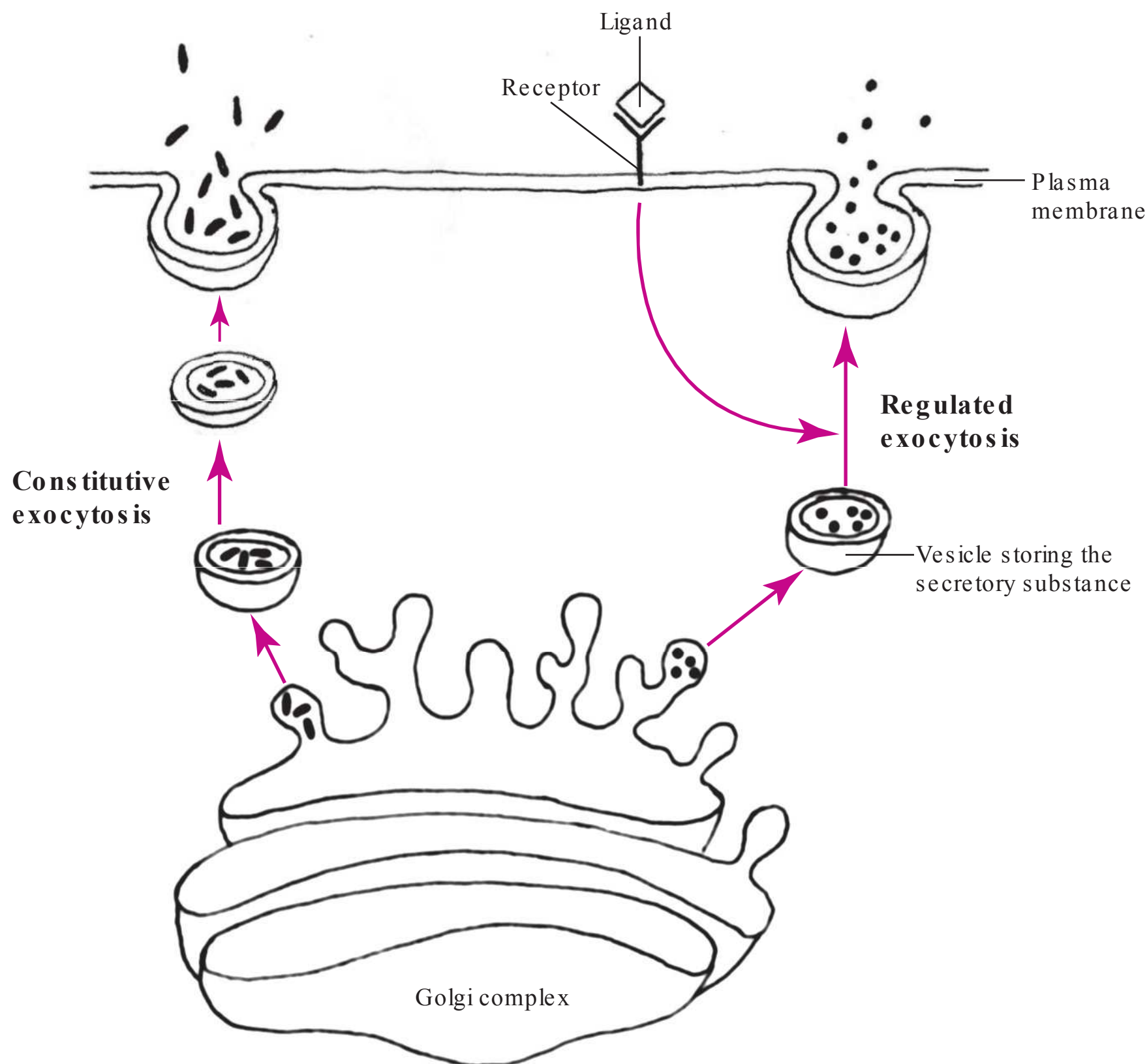
**Figure 3.4** Receptor-mediated endocytosis.

## Exocytosis

- It is the process by which secretory and undigested materials are expelled outside the cell, into the extracellular space.



- Materials which are removed from the cell are present in membrane-bound vesicles. The membrane of the vesicle fuses with the cell membrane and contents of the vesicle are released into the extracellular space.
- There are two types of exocytosis:
  - Regulated exocytosis (Fig. 3.5):** In this process, the substance is stored temporarily in the vesicle within the cytoplasm. The release of the substance from the vesicle is triggered by an extracellular signal.
  - Constitutive exocytosis (Fig. 3.5):** In this process, there is no temporary storage. The substance is released immediately after synthesis. The release of the substance is continuous, and it is not dependent on the extracellular signal.



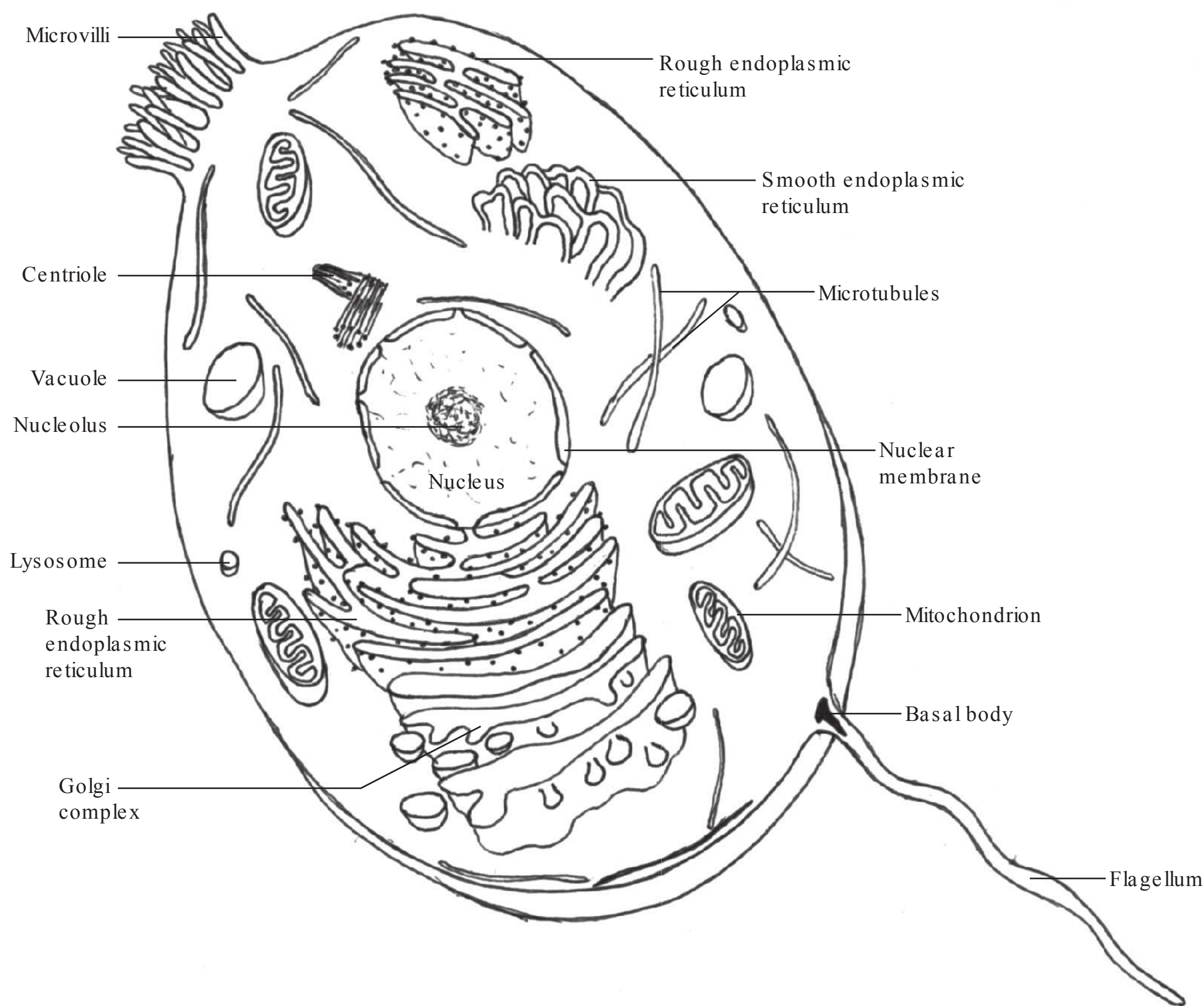
**Figure 3.5** Pathways of exocytosis.

## CYTOPLASM

- The cytoplasm is a gel-like fluid present between the plasma membrane and the nucleus of the cell.
- Cytoplasmic organelles, cytoplasmic inclusions and cytoskeletons are the three main components of the cytoplasm.
  - Cytoplasmic organelles are small organs within the cell which are involved in metabolism. For example, mitochondria and endoplasmic reticulum.
  - Cytoplasmic inclusions are small particles seen temporarily in the cytoplasm. They may or may not be membrane-bound, and are metabolically inactive. For example, lipid droplets, glycogen granules and pigment granules.
  - Cytoskeletons provide the structural framework to the cell.

**CELL ORGANELLES (Fig. 3.6)**

Cell organelles are classified as membranous, that is membrane-bound, and non-membranous. They are listed in Table 3.1.



**Figure 3.6** Ultrastructure of a cell showing cell organelles.

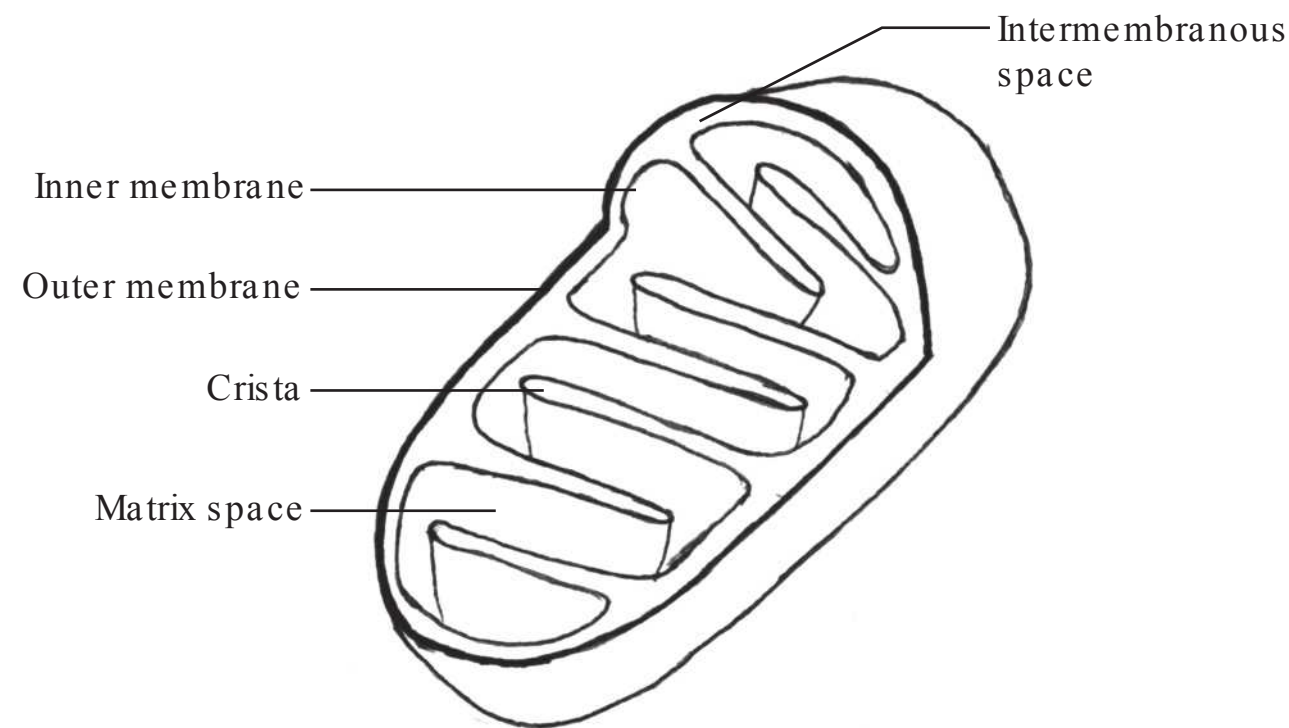
**Table 3.1** Cell Organelles

Membranous cell organelles	Non-membranous cell organelles
<ul style="list-style-type: none"><li>• Golgi complex</li><li>• Endoplasmic reticulum—rough and smooth</li><li>• Mitochondria</li><li>• Lysosomes</li><li>• Peroxisomes</li><li>• Endosomes</li></ul>	<ul style="list-style-type: none"><li>• Ribosomes</li><li>• Cytoskeleton—microtubules, microfilaments and intermediate filaments</li></ul>

**Mitochondria (Singular: Mitochondrion)**

- These ovoid-shaped structures are bounded by the phospholipid bilayer. The outer membrane is smooth and encloses the entire organelle, and the inner membrane encloses the inner space called matrix space. The space between the two membranes is intermembrane space (Figs 3.6 and 3.7).





**Figure 3.7** Mitochondrion.

- The inner membrane is folded to form cristae (singular: crista) (Fig. 3.7). The inner membrane contains the molecules of the electron transport chain and adenosine triphosphate (ATP) synthase.
- The matrix space is filled with mitochondrial matrix. The matrix contains matrix granules, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), ribosomes and all the enzymes of Krebs's cycle except succinate dehydrogenase, which is on the inner membrane.
- Functions: It is the site for synthesis of ATP, which is the source of energy. Hence, the mitochondria are also called 'powerhouses' of the cell.

### Ribosomes

- These are complexes of ribosomal ribonucleic acid (rRNA) and proteins.
- Ribosomes consist of two subunits, small (40S) and large (60S), classified on the basis of their sedimentation rates.
- They are present in two forms: they may be free in the cytoplasm or may be studded on the rough endoplasmic reticulum (RER) or outer nuclear membrane (Fig. 3.6).
- Clusters of ribosomes bound to a single strand of messenger RNA (mRNA) are called polyribosomes or polysomes.
- Function: They are the sites for protein synthesis, and translation of mRNA into protein occurs in the ribosomes. Free ribosomes have a role in the synthesis of proteins that are used within the cell.

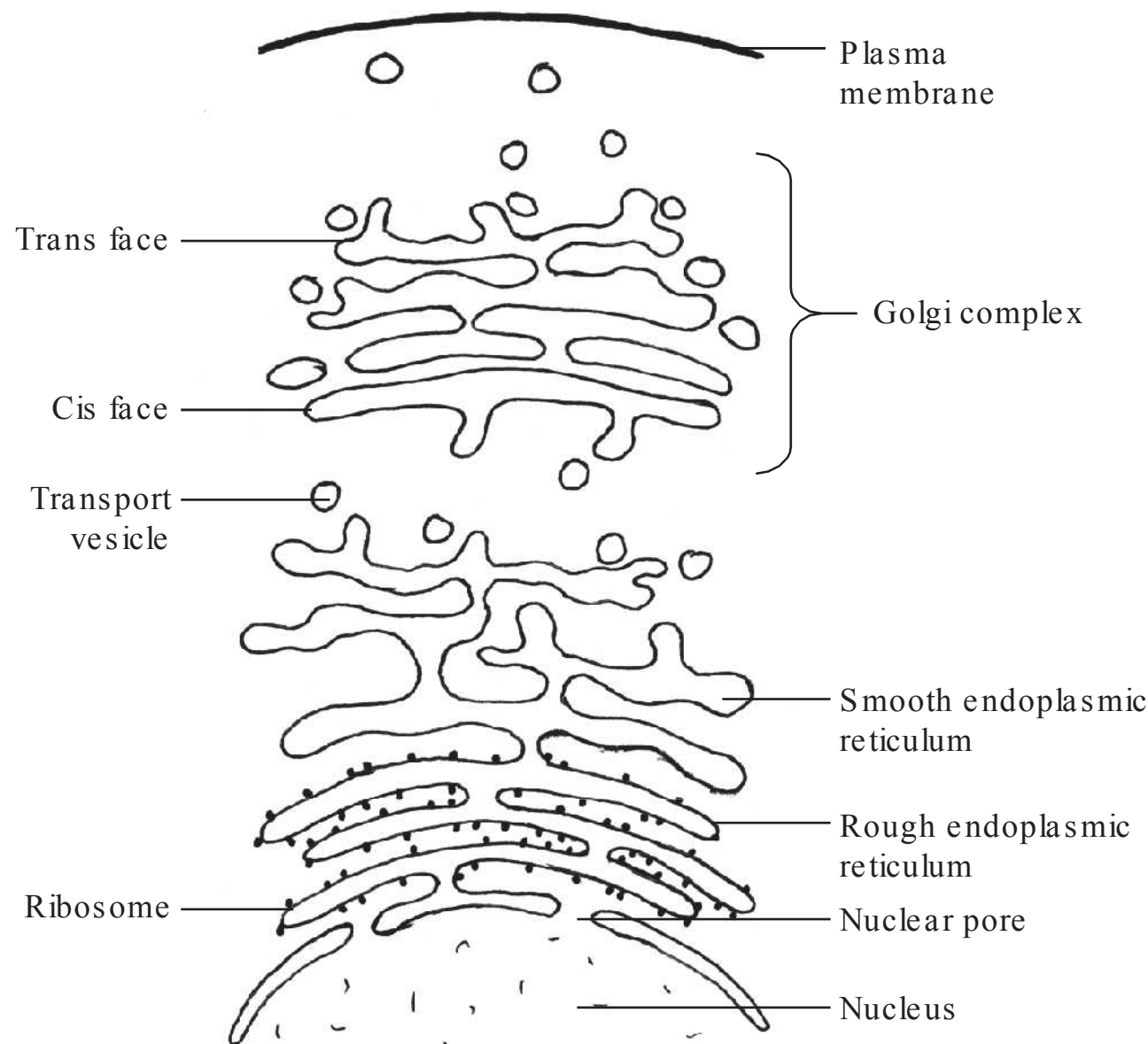
### Endoplasmic Reticulum

Endoplasmic reticulum (ER) is a network of folded membranes that form vesicles and cisternae (singular: cisterna). There are two types of endoplasmic reticulum:

#### 1. Rough endoplasmic reticulum

- Ribosomes are present on its outer surface, giving it a rough appearance (Figs 3.6 and 3.8).
- The membrane of some RERs is continuous with outer nuclear membrane.
- The membrane-bound flattened sacs are known as cisternae.
- Proteins formed by ribosomes enter the RER.
- The membrane of the RER breaks off to form protein-filled sacs known as vesicles. A vesicle is a transport vehicle for the protein through which the protein reaches the Golgi body for further processing.
- Functions: It is the site for protein synthesis. Proteins are synthesised by ribosomes present on the external surface of the RER.





**Figure 3.8** Golgi complex and rough and smooth endoplasmic reticulum.

## 2. Smooth endoplasmic reticulum

- Smooth endoplasmic reticulum (SER) is an irregular network of folded membranes that are devoid of ribosomes; hence, they appear smooth (Figs 3.6 and 3.8).
- SERs are abundant in cells which synthesise steroids, such as Leydig cells of the testis and cells of the adrenal cortex. They are also abundant in liver cells and help in detoxification of drugs.
- Functions: They are involved in the synthesis of lipids and steroid hormones. They contain enzymes that help detoxify certain drugs.

## Golgi Complex

- It is composed of stacks of membrane-bound flattened structures known as cisternae (Figs 3.6 and 3.8).
- There are numerous small vesicles around the stack.
- The cis face of the Golgi complex is the cisterna, nearest to the RER. It receives the transport vesicles of proteins synthesised in RER.
- The trans face is opposite to the cis face, away from the RER. Secretory vesicles are formed here.
- Between the cis and trans faces, there is the medial compartment of the Golgi complex; in this part of the Golgi complex, carbohydrate components are added to the proteins and lipids.
- Functions: It is involved in modifying, sorting and packaging of secretory products.

## Lysosomes

These are membrane-bound spherical vesicles present in all cells (Fig. 3.6). Their function is intracellular digestion, and they contain hydrolytic enzymes that are involved in degradation of macromolecules. They are present in large numbers in phagocytic cells. They degrade the bacterium (plural: bacteria) that has been phagocytosed by the phagocytic cells. Lysosomes are present in three forms: primary, secondary and tertiary.

### 1. Primary lysosomes

- Newly formed lysosomes, having inactive enzymes, are called primary lysosomes.

## 2. Secondary lysosomes

- Within the phagocytic cell, primary lysosomes fuse with phagosomes and lysosomal enzymes become active; now these lysosomes are called secondary lysosomes.

## 3. Tertiary lysosomes

- Bacterium gets degraded by the actions of lysosomal enzymes. The vesicle containing degraded bacterium is now called residual body or tertiary lysosome.
- No enzymatic activity is seen in tertiary lysosomes.
- The leftover products of digestion after fusion with the contents of lysosomes are referred to as residual bodies.
- Lipofuscin granules are the residual bodies present in old cells. These granules contain brown pigment granules which are lipid-containing residues of lysosomal degradation.

## Endosomes

- Endosomes are membrane-bound compartments in which the endocytosed substance is stored before they undergo lysosomal degradation.
- They consist of tubules and vesicles and are located near the plasma membrane.

## Peroxisomes

- Peroxisomes are membrane-bound organelles which contain enzymes.
- They are involved in oxidation of long-chain fatty acids.
- Certain enzymes of peroxisomes oxidise various substrates to hydrogen peroxide, which is bactericidal. The enzyme catalase converts the excess hydrogen peroxide, which is toxic, into water.

## CYTOSKELETON

- It is a network of protein filaments in the cytoplasm of a cell.
- It provides structural framework to the cells. It also helps in cell movement and movement of cytoplasmic components during several processes such as phagocytosis, endocytosis and exocytosis.
- It consists of three main components: microfilaments, microtubules and intermediate filaments.

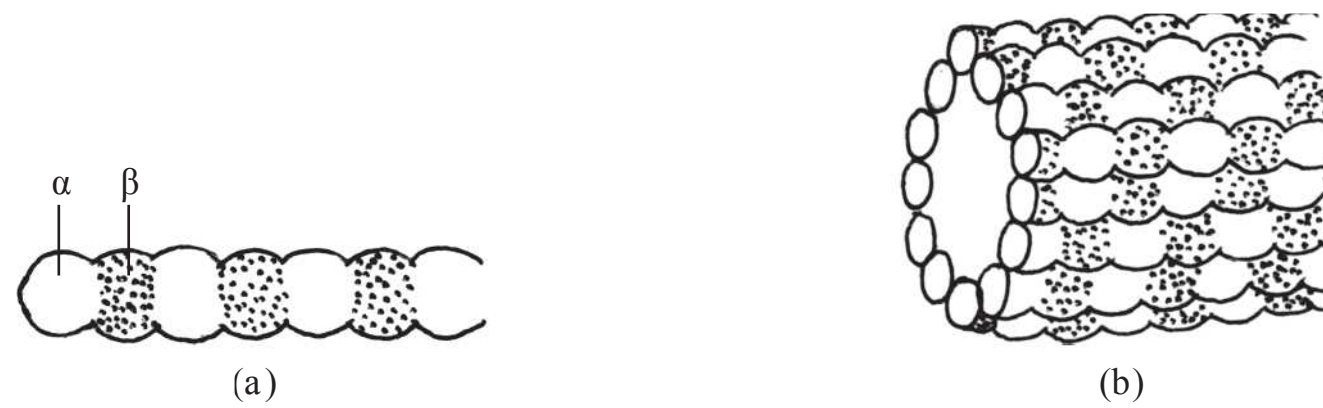
## Microfilaments

- Microfilaments are composed of fine filaments of the protein actin.
- In the skeletal muscle, actin filaments interact with another filamentous protein, myosin, and bring about contraction of the muscle.
- Actin filament provides structural support to microvilli (for structure of microvilli, refer to Chapter 4).
- Microfilaments are involved in several cellular processes such as phagocytosis, endocytosis and cell movement.

## Microtubules

- Microtubules are hollow tubules; the wall of the tubule is composed of the protein tubulin.
- Each microtubule is made up of 13 protofilaments of tubulin protein (Fig. 3.9).
- Protofilaments consist of tubulin subunits. Each tubulin subunit consists of  $\alpha$ - and  $\beta$ -subunits.
- The microtubule is an important component of centriole, cilia and flagella. The centriole is composed of nine microtubule triplets. Cilia and flagella are composed of nine doublets oriented around two additional microtubules (9 + 2 arrangement).
- Functions: Microtubules help in maintenance of cell shape, intracellular transport and formation of mitotic spindles during mitosis.

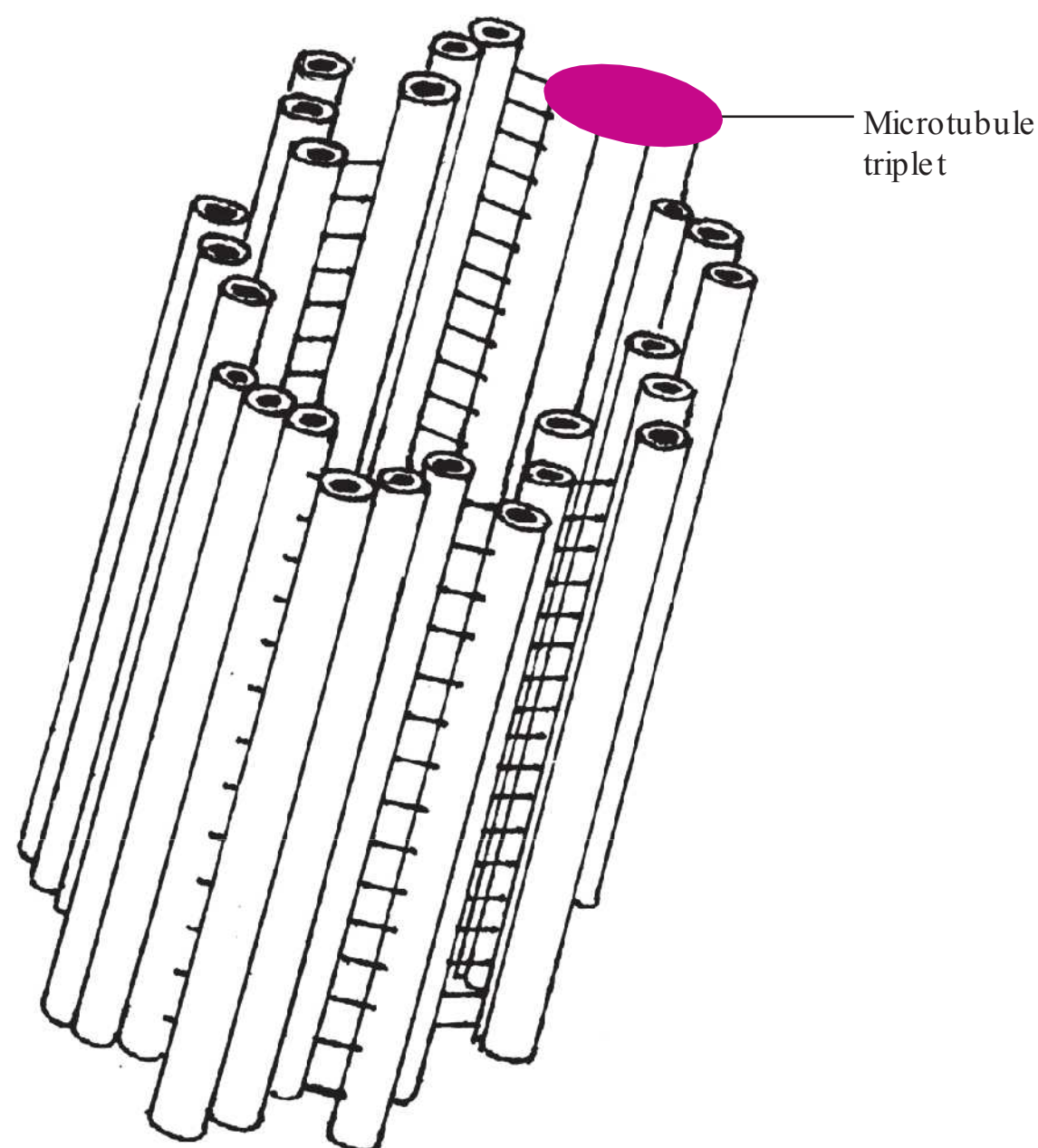




**Figure 3.9** (a) Protofilament, which consists of tubulin subunits ( $\alpha$  and  $\beta$ ), and (b) microtubule. Thirteen protofilaments constitute a microtubule.

### Centriole

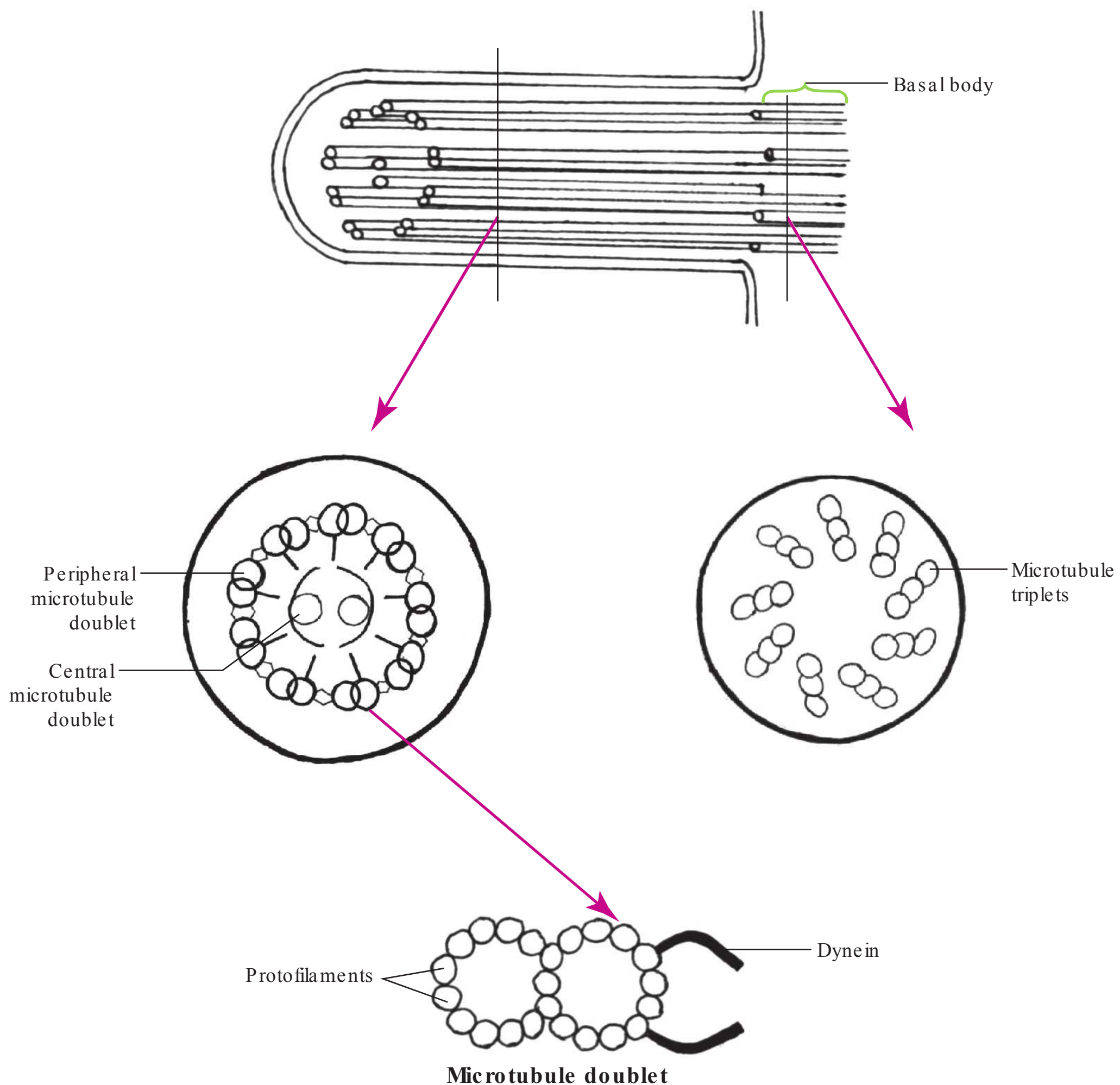
- Its wall consists of nine subunits (Fig. 3.10).
- Each subunit consists of three (triplets) microtubules.
- Centrioles duplicate just before cell division.
- Centrioles are present in pairs, arranged at right angles to each other. They are located near the nucleus and are often surrounded by Golgi complexes.
- Functions: They form basal bodies of cilia and flagella (described in the following text). Centrioles organise the microtubules during both mitotic and resting phases of a cell.



**Figure 3.10** Centriole showing nine microtubule triplets.

### Cilia (Singular: Cilium)

- Cilia are elongated, motile evaginations from the cell surface.
- Each cilium arises from a basal body.
- The basal body is similar to centriole with nine subunits of microtubules, each subunit consisting of triplets of microtubules (Fig. 3.11).
- The core of each cilium consists of longitudinally arranged parallel microtubules, which are known as axoneme.



**Figure 3.11** Structure of a cilium.

- The microtubules of axoneme are extensions of the two innermost microtubules of the triplets of the basal body. Hence, the axoneme has nine doublets of microtubules. It also has two central microtubules (Fig. 3.11).
- The arrangement of microtubules in the basal body is '9 + 0' and in the shaft of the cilia is '9 + 2'.
- Neighbouring doublets of microtubules are linked to each other by the protein nexin.
- Arms extending from each microtubule of doublets consist of the protein dynein (Fig. 3.11).
- Each doublet in the periphery is connected to the central pair of microtubules by radial spokes.
- Functions: Cilia help in propelling the liquid material present on the surface of the cell.

### Intermediate Filaments

- Intermediate filaments are one of the three cytoskeletal filaments.
- They provide tensile strength to the cells.
- There are several types of intermediate filaments. Keratins are found in epithelial cells, nuclear lamins form a network that stabilises the nuclear envelope and neurofilaments support the axons of neurons.



## NUCLEUS

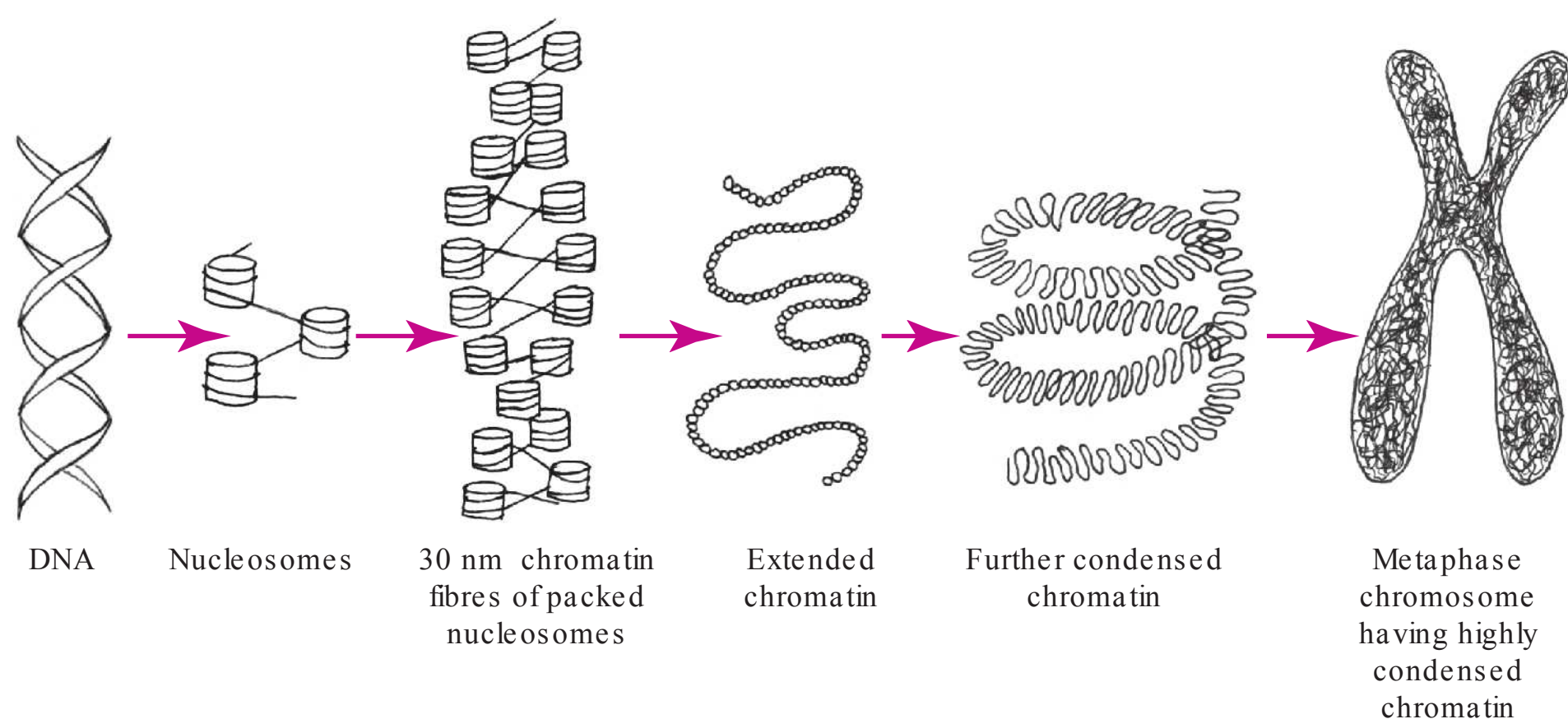
- It is the largest cell organelle.
- It is present in most of the cells (absent in mature erythrocytes and platelets). Generally, there is one nucleus per cell, but some cells may have more than one, for example, skeletal muscle cells, osteoclasts and a few cells in transitional epithelium.
- The shape of the nucleus varies in different types of cells—it may be spherical, flat, elongated or lobulated.
- It serves to store and organise genetic information and controls the entire metabolic process of a cell.
- It consists of various parts: nuclear membrane, chromatin, nucleolus and nucleoplasm.

### NUCLEAR MEMBRANE

- Nuclear membrane separates the nuclear material from the cytoplasm.
- It consists of two layers of lipid bilayer; the two membranes are separated by a narrow intermembranous space called perinuclear cisterna.
- The outer layer is studded with ribosomes and it is continuous with RER.
- The inner and outer layers fuse to form nuclear pores.

### CHROMATIN

- Chromatin consists of the DNA of the nucleus and the associated proteins (mostly histones).
- It is present in two forms: heterochromatin and euchromatin.
- Heterochromatin appears dense, is located in the periphery of the nucleus and is transcriptionally inactive.
- Euchromatin is a lightly stained, transcriptionally active form.
- The chromatin is organised in a particular way to form chromosomes.
- The fundamental structural unit of chromatin is a nucleosome (Fig. 3.12). DNA wrapped around the histones forms a nucleosome. The portion of DNA joining adjacent nucleosomes is known as linker DNA.



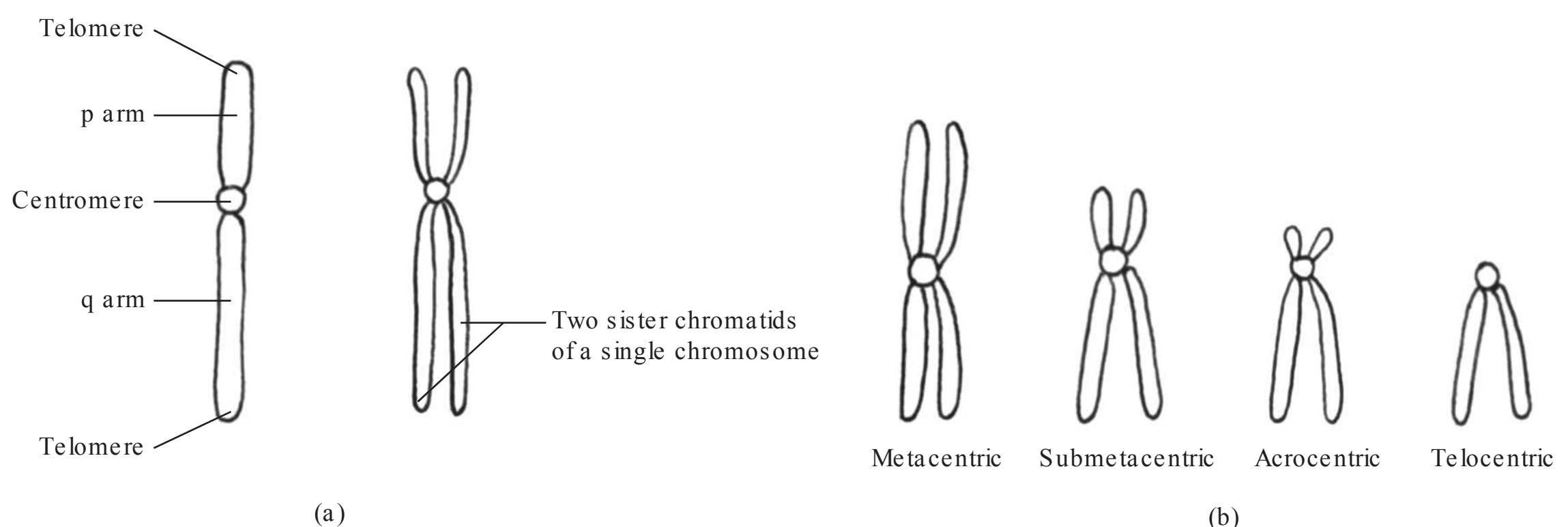
**Figure 3.12** Packing of chromatin.



- Nucleosomes coil around an axis to form chromatin fibres each with a diameter of 30 nm. There are six nucleosomes per coil in 30-nm chromatin fibres.
- Chromatin fibres are further folded into a series of successively higher order packing to eventually form a compact structure, the chromosome (Fig. 3.12).

### Chromosomes (Fig. 3.13)

- A chromosome consists of a highly folded and condensed single DNA molecule. The associated proteins help in organisation of the DNA.
- Chromosomes are best seen during cell division when they reach maximum condensation.
- Each chromosome consists of a short arm (p) and a long arm (q); they are connected to each other by a constricted region known as centromere.
- After DNA replication, chromosomes consist of a pair of identical chromatids joined by a centromere. The tips of the chromosome arms are known as telomeres.
- Based on the position of centromeres, chromosomes are classified into the following types:
  - (a) Metacentric: This is a chromosome with a centrally placed centromere. Both arms of the chromosome are almost equal in length.
  - (b) Submetacentric: This is a chromosome whose centromere lies between its centre and its end; hence, in such chromosomes arm lengths are unequal.
  - (c) Acrocentric: This is a chromosome whose centromere is located very close to one end so that the p arm is very small.
  - (d) Telocentric: This is a chromosome whose centromere is located at the end.



**Figure 3.13** Chromosome showing (a) parts and (b) types.

- During cell division, a protein complex known as kinetochore assembles at the centromere. The microtubules of the mitotic spindle get attached to the kinetochore.
- In humans, all somatic cells have 23 pairs of chromosomes, each pair having one chromosome from each parent. Twenty-two pairs of chromosomes are autosomes and a single pair are sex chromosomes. Sex chromosomes are XX in females and XY in males.
- Homologous chromosomes are a pair of chromosomes carrying the same genetic information. The pair has one chromosome from each parent.

## NUCLEOLUS

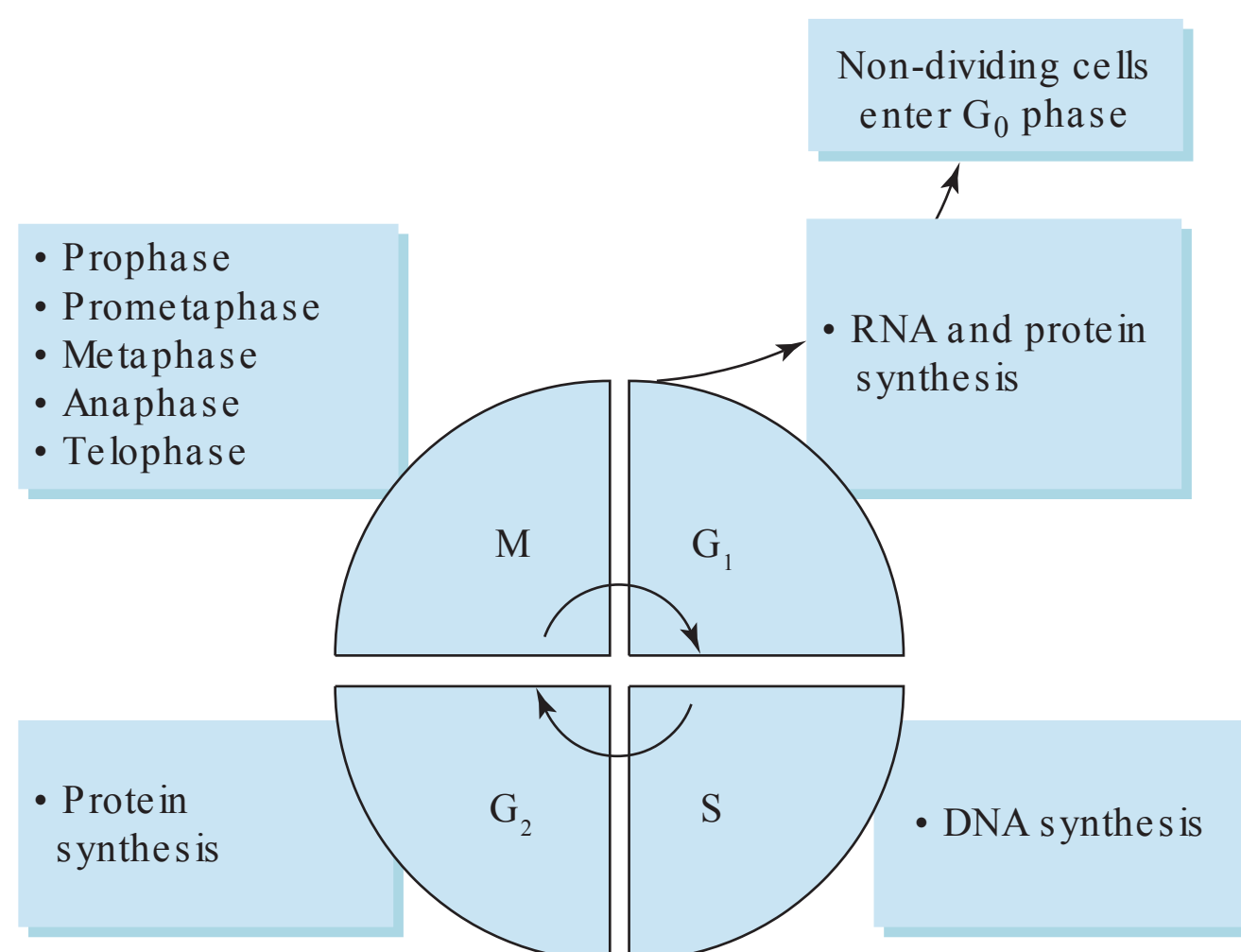
- It is a spherical, non–membrane-bound structure inside the nucleus.
- Each cell has one or two nucleoli.
- It consists of ribosomal RNA (rRNA) and proteins.
- It is the site of rRNA synthesis.

## NUCLEOPLASM

Nucleoplasm is a viscous fluid inside the nucleus that surrounds the nucleoli and chromatin.

## CELL CYCLE

- An actively dividing cell goes through a series of stages; together these stages are known as cell cycle.
- The entire cell cycle is divided into two main stages: mitosis (M phase) and interphase (Fig. 3.14).
- All somatic cells undergo mitotic cell division, whereas germ cells undergo meiotic cell division.



**Figure 3.14** Cell cycle.

## INTERPHASE

The interphase is the period between two successive cell divisions; it includes G<sub>1</sub>, S and G<sub>2</sub> phases (Fig. 3.14). The non-dividing cells such as mature erythrocytes and neurons are in a phase known as G<sub>0</sub> phase.

### 1. G<sub>1</sub> phase

- G<sub>1</sub> phase stands for Gap 1 phase.
- This phase begins immediately after mitosis. It is a phase of cellular growth.
- The cell increases in size, and RNA and protein synthesis takes place. There is no DNA synthesis in this phase.
- At a certain point during this phase (checkpoint), the cell enters S phase.

### 2. S (synthesis) phase

- DNA and protein synthesis occurs in this phase.
- There is replication and doubling of DNA.
- Each chromosome now consists of two sister chromatids, each of which has identical DNA.
- This phase lasts for 8–10 hours.

### 3. G<sub>2</sub> phase

- It is the phase between DNA synthesis (S phase) and mitosis (M phase).
- Proteins synthesised during this phase are required during mitosis.

## MITOSIS

It consists of karyokinesis (nuclear division) and cytokinesis (division of cytoplasm). At the end of mitosis, two identical daughter cells are produced. The duration of this phase is much shorter than interphase. It lasts for 2–3 hours. Mitosis consists of five phases: prophase, prometaphase, metaphase, anaphase and telophase.

#### 1. Prophase (Fig. 3.15)

- Condensation of chromatin begins in this phase, which results in formation of two sister chromatids. The two parallel sister chromatids are attached to the centromere.
- The nucleolus disappears.
- Two pairs of centrioles move gradually to the opposite poles of the cell.
- Formation of mitotic spindle begins.

#### 2. Prometaphase (Fig. 3.15)

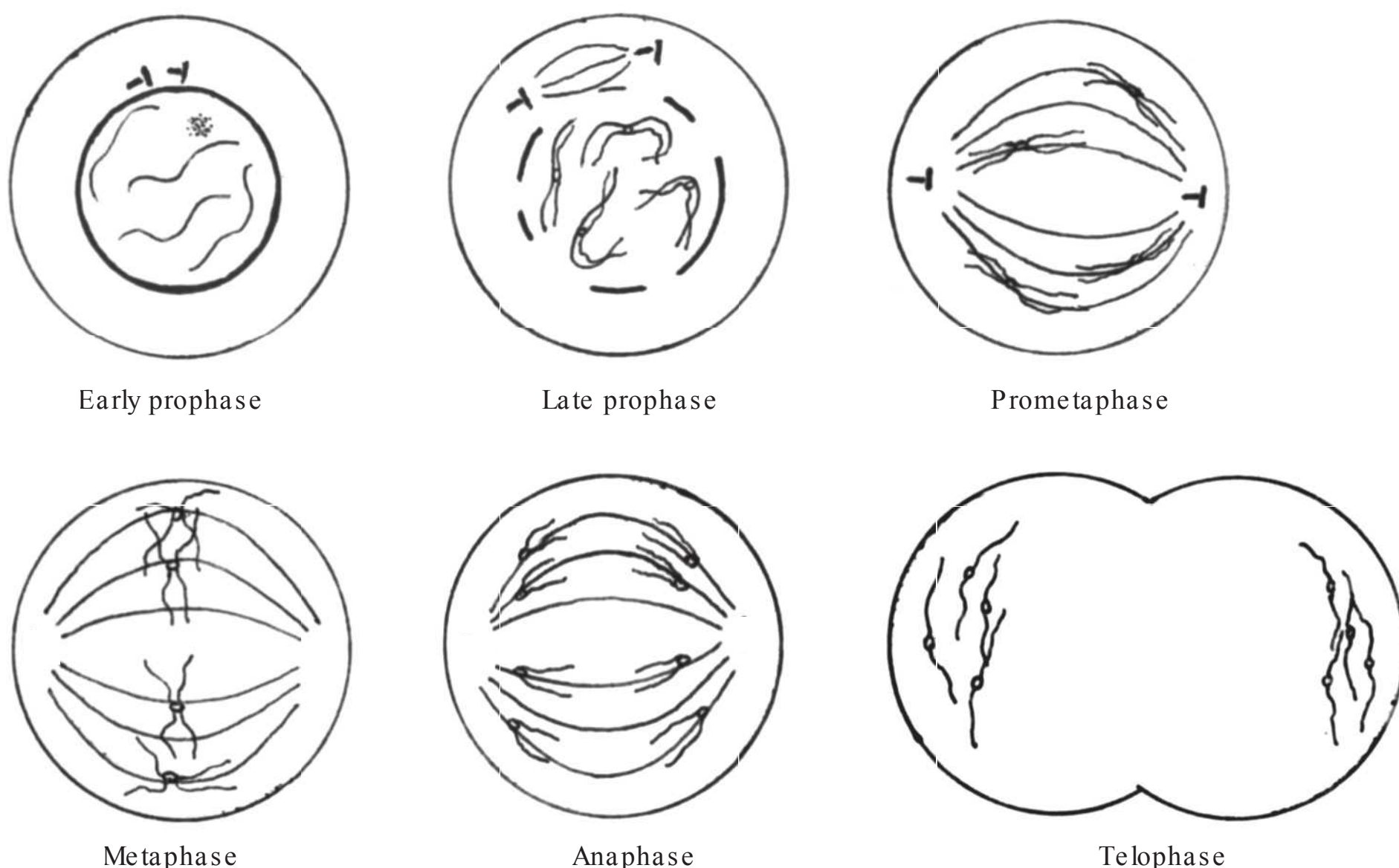
- Condensation of chromatin continues.
- Nuclear membrane disintegrates and chromosomes disperse in the cytoplasm of the cell.
- Microtubules of the mitotic spindle attach to the kinetochore of the chromosomes.
- Chromosomes start moving towards the centre of the spindle.

#### 3. Metaphase (Fig. 3.15)

- Chromosomes reach maximum condensation during this phase.
- Chromosomes line up at the equatorial plate of the cell between the two opposite poles of the spindle.

#### 4. Anaphase (Fig. 3.15)

- The sister chromatids separate at the centromere.
- Each sister chromatid now becomes a daughter chromosome.
- The daughter chromosomes begin to move towards the opposite poles of the cell.



**Figure 3.15** Phases of mitosis.



### 5. Telophase (Fig. 3.15)

- Uncoiling of chromosomes begins.
- Chromosomes separate from the microtubules of the spindle.
- A nuclear membrane appears around each of the two groups of daughter chromosomes.
- Cleavage of the cytoplasm gives rise to two daughter cells.
- The nucleolus appears.
- The daughter cells now enter  $G_1$  phase of the cell cycle.

## MEIOSIS

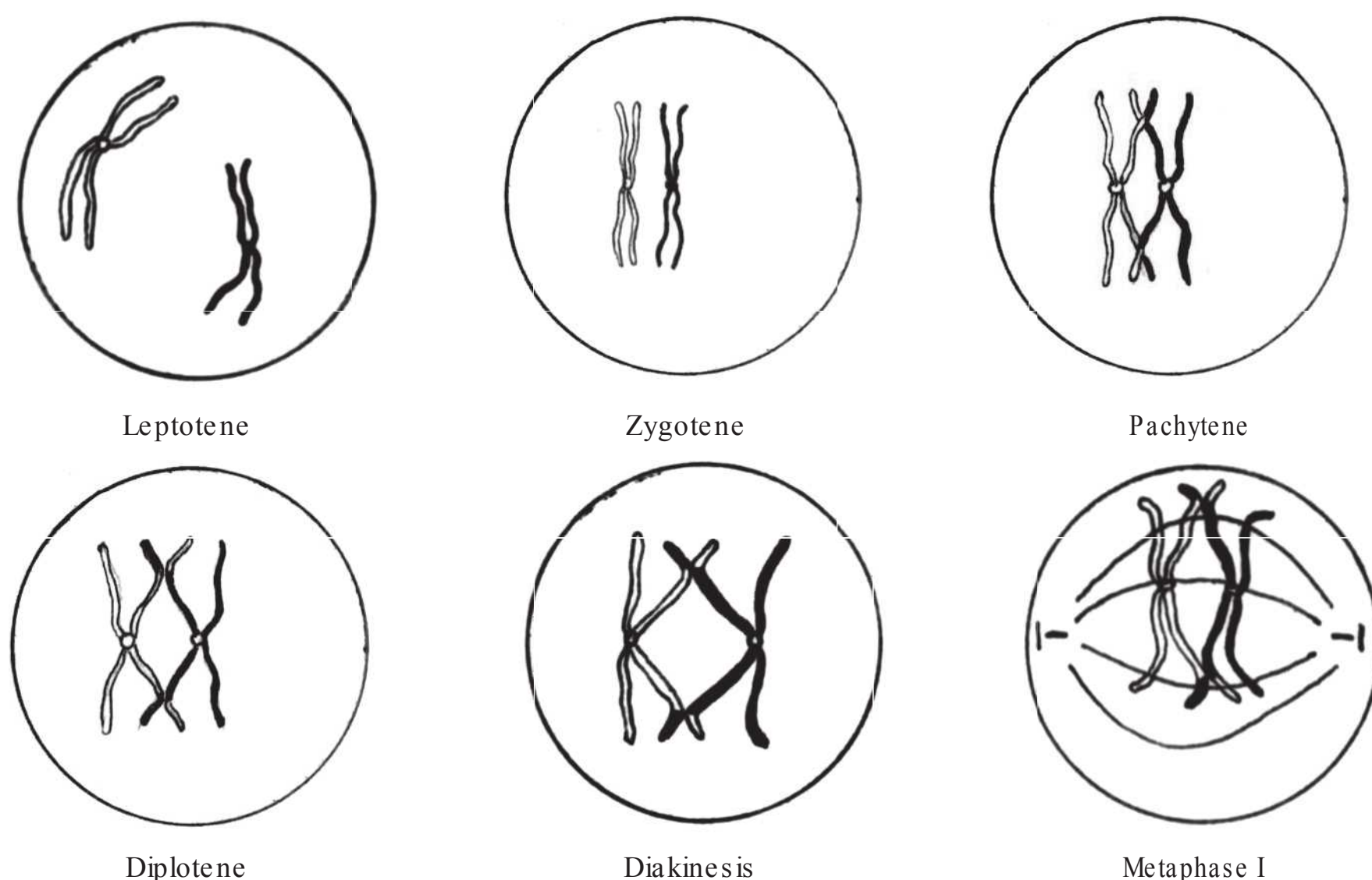
- Meiosis is a specialised cell division resulting in daughter cells with half the genetic material of the parent cell.
- It occurs in diploid germ cells and gives rise to haploid gametes.
- Meiosis consists of two successive cell divisions known as meiosis I and meiosis II.

### Meiosis I

- Meiosis I is also known as reduction division, because the number of chromosomes is reduced by half in the daughter cells produced after meiosis I.
- As in mitosis, meiosis is also preceded by the interphase, during which DNA content is doubled.

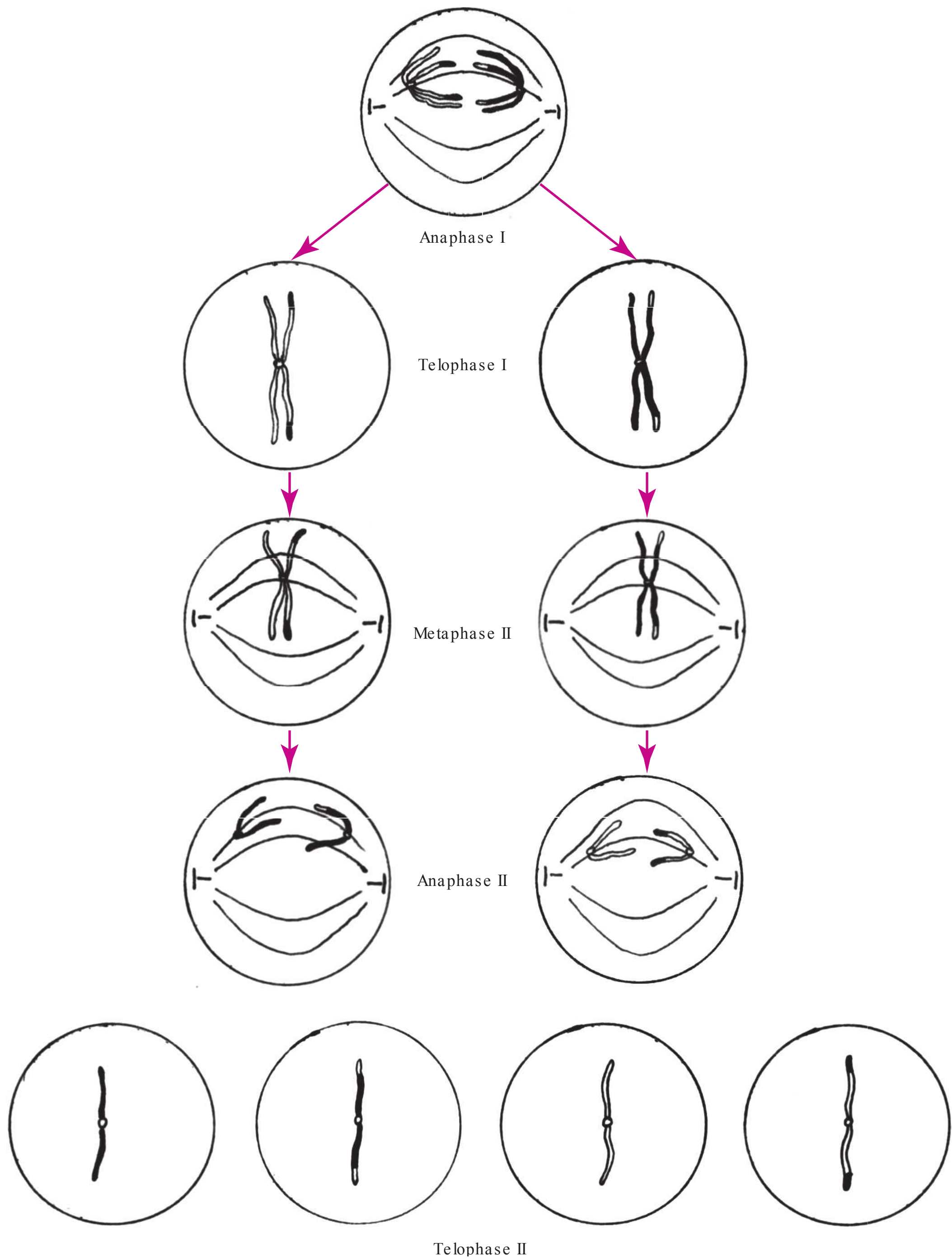
#### Prophase I (Fig. 3.16)

- Prophase I consists of the following stages:
  - (a) Leptotene: The DNA of the cell entering this phase is already duplicated (duplication occurs during interphase). In this phase, chromosomes begin to condense.
  - (b) Zygotene: Pairing of homologous chromosomes occurs in this phase. Homologous chromosomes align close to each other along their entire length. Four chromatids of two homologous chromosomes are called bivalent or tetrad. Homologous chromosomes are held together by the synaptonemal complex. Chromosomal condensation continues.
  - (c) Pachytene: Crossing-over takes place during this phase. Homologous regions are exchanged between non-sister chromatids of the homologous chromosomes.



**Figure 3.16** Phases of meiosis. (continued)





**Figure 3.16** (continued) Phases of meiosis.

- (d) Diplotene: Separation of homologous chromosomes begins. However, they remain attached in the regions where crossing-over took place; these regions are known as chiasmata.
- (e) Diakinesis: Chromosomes reach maximum condensation. The nucleolus disappears and nuclear membrane begins to disintegrate. Spindle formation begins.

Metaphase I (Fig. 3.16)

- The homologous pairs of chromosomes line up at the equatorial plate of the cell between the two opposite poles of the spindle.

Anaphase I (Fig. 3.16)

- In this phase, homologous chromosomes move apart towards the opposite poles of the cell with their sister chromatids.
- Each set of chromosomes has the half number of chromosomes.

Telophase I (Fig. 3.16)

- Cleavage of the cytoplasm gives rise to two daughter cells (secondary oocytes or spermatocytes) with haploid chromosomes.
- Each chromosome still has a pair of sister chromatids attached to the centromere.
- Due to crossing over, the chromosomes of the two daughter cells are not identical.

Meiosis II (Fig. 3.16)

- Meiosis II is similar to mitosis. During meiosis II, the sister chromatids separate at the centromere.
- At the end of meiosis II, four haploid cells (spermatids or ova) are formed. The chromosomes of all four cells are non-identical.

KEYPOINTS

Cell Organelles

Cell organelle	Basic structure	Function
Mitochondria	They are bound by the phospholipid bilayer; the outer wall is smooth and inner membrane is folded to form cristae	Site for ATP synthesis
Ribosomes	They are complexes of ribosomal ribonucleic acid (rRNA) and proteins	Protein synthesis
Rough endoplasmic reticulum	It has ribosomes on its outer surface	Protein synthesis
Smooth endoplasmic reticulum	They are a network of folded membranes that are devoid of ribosomes	Synthesis of lipids and steroid hormones
Golgi complex	It is composed of stacks of membrane-bound flattened structures known as cisternae	Modifying, sorting and packaging of secretory products
Lysosomes	They are membrane-bound spherical vesicles	Intracellular digestion

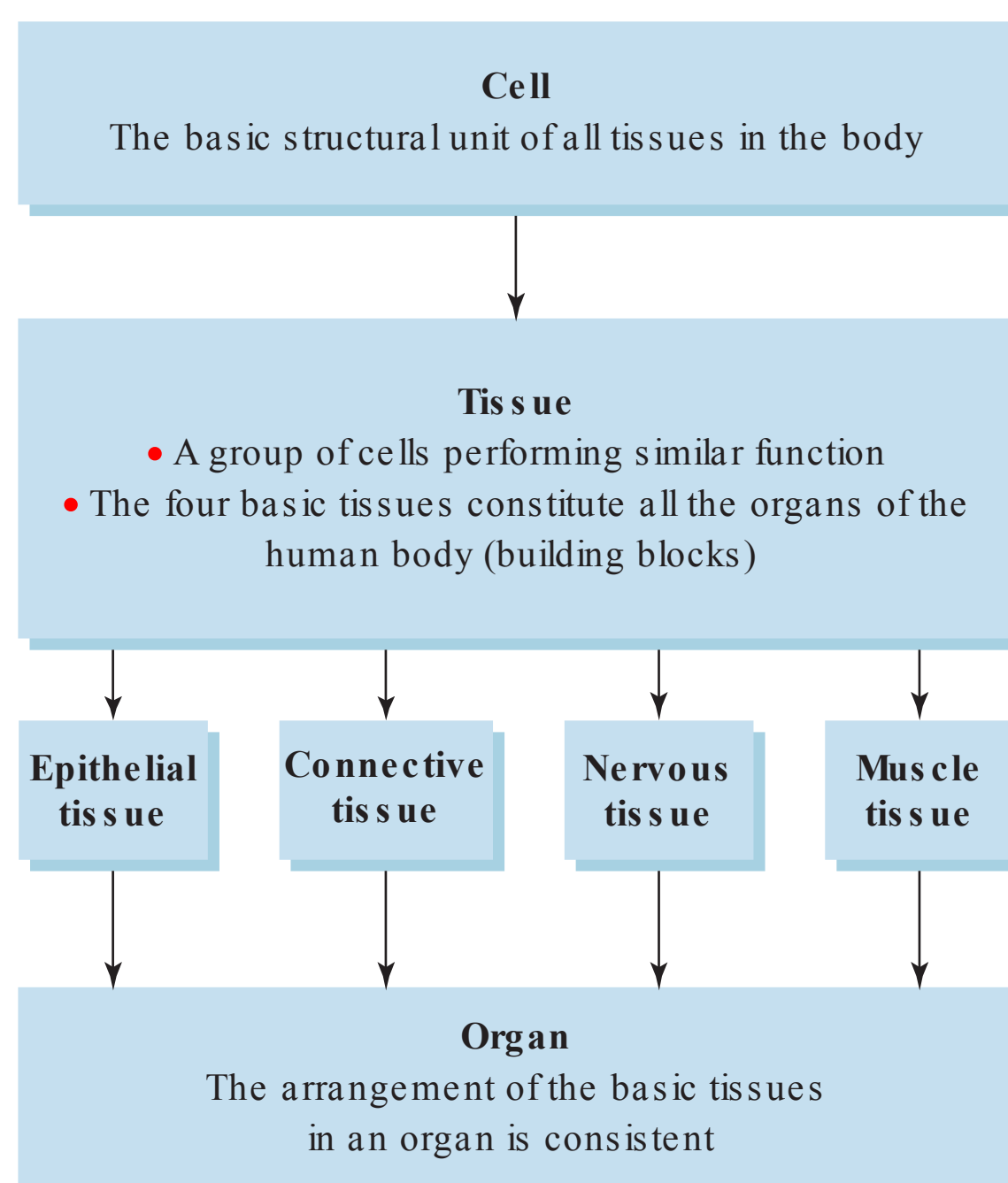
SELF-ASSESSMENT

1. Describe the structure of plasma membrane.
2. Describe active and passive transport.
3. Describe the structure and function of endoplasmic reticulum.
4. Describe the structure of cilia.

# Epithelia and Glands

### STRUCTURAL ORGANISATION OF THE HUMAN BODY

- All the organs of the human body are built of four basic tissues (Fig. 4.1) which are as follows:
  - (a) Epithelial tissue
  - (b) Connective tissue
  - (c) Nervous tissue
  - (d) Muscle tissue
- The arrangement of these tissues in an organ is consistent.
- This chapter discusses the epithelial tissue; the rest of the tissues are discussed in subsequent chapters.



**Figure 4.1** Structural organisation of the human body.



## EPITHELIAL TISSUE

- Epithelial tissue covers the body and lines the inner and outer surfaces of the organs and the body cavities.
- Epithelia (singular: epithelium) are tissues composed of tightly packed cells with very little intercellular substance. They lie on a thin basement membrane which separates the epithelium from the connective tissue (see Figs 4.3 and 4.4). The major components of the basement membrane are glycoproteins and collagen. The basement membrane is described in more detail in Chapter 5.
- Epithelia are themselves avascular but are present on an underlying layer of vascular connective tissue, the lamina propria. The metabolites and oxygen diffuse through the lamina propria to the epithelium.
- When epithelium is moistened by secretions of mucous glands present in the epithelium or lamina propria, the two together (epithelium and lamina propria) are called mucosa, for example, in the lining of intestines and genital and urinary tracts.
- Since the epithelial cells have good capacity of regeneration, they undergo mitosis and replace damaged cells with new cells.
- The epithelial tissue is derived from all the three germ layers:
  - (a) The epidermis of the skin is derived from ectoderm.
  - (b) Lining epithelia of digestive and respiratory tracts are derived from endoderm.
  - (c) Mesoderm gives rise to the lining epithelium of the vascular system and the mesothelium lining the peritoneal, pericardial and pleural cavities.

## FUNCTIONS OF EPITHELIA

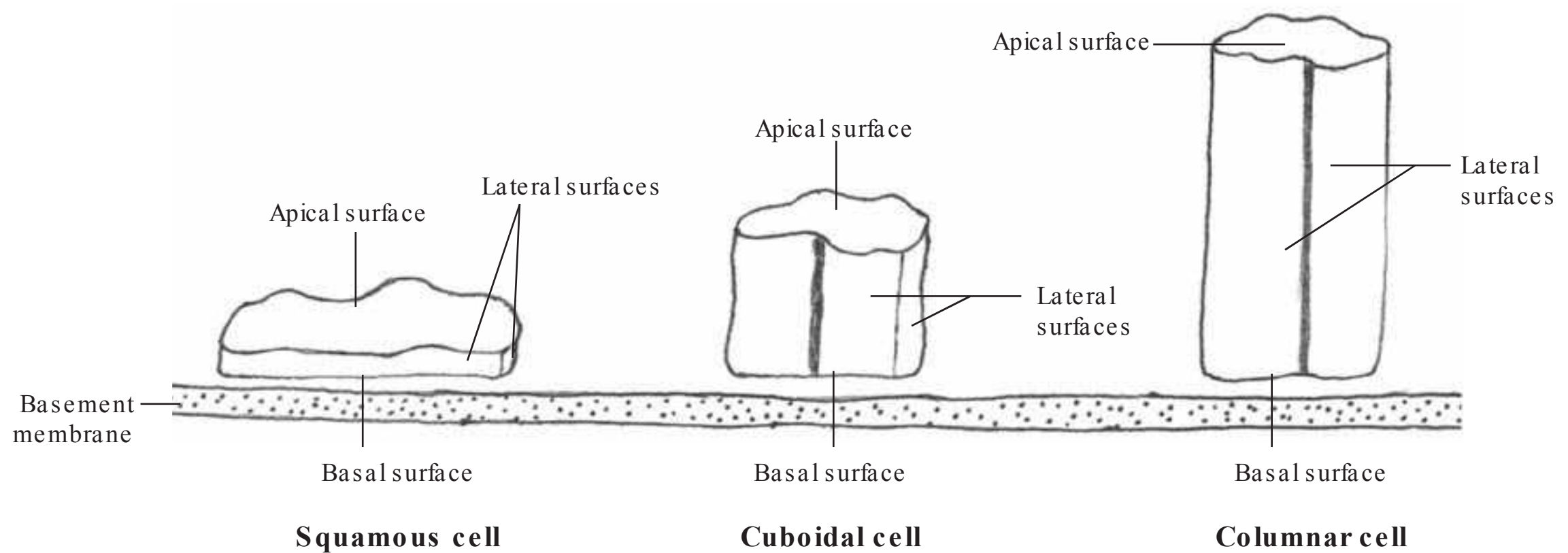
Cells of an epithelium can perform a variety of functions. Major functions of epithelia are as follows:

1. **Protection and barrier:** The epithelium covers the entire external and internal surfaces of the body and forms a barrier; anything that enters or exits the body has to cross this barrier. The epithelium of the skin protects the body from mechanical injury and invasion of microorganisms. It also prevents excessive loss of water.
2. **Absorption:** The epithelium of the intestine is involved in absorption of water and digested food from the lumen of the intestine.
3. **Secretion:** The secretory cells of all glands are derived from epithelium. These secretory cells synthesise and release secretory products.
4. **Selective permeability:** The epithelium permits the passage of certain substances through the epithelial layer. For example, gaseous exchange between alveolar air and the blood in the pulmonary capillaries occurs because the epithelia lining them allow the passage of gases.
5. **Sensory perception:** Specialised epithelial tissue in sense organs, innervated by sensory nerve endings, helps in sensory perception.
6. **Excretion:** Epithelia of the kidney tubules excrete waste products from the body. The epithelial cells of the sweat glands excrete sweat from the body.

## EPITHELIAL CELLS

- In general, three different shapes of cells are seen in epithelia—squamous, cuboidal and columnar (Fig. 4.2) (described in more detail under simple epithelium). Apart from these three basic shapes of the epithelial cells, some epithelia have cells which are different from these three; they are described later under that particular epithelium.
- Epithelial cells have three surfaces: a basal surface which is in contact with the basement membrane, an apical surface facing the surface of the epithelium and a lateral surface which is in contact with the same surface of the neighbouring epithelial cells (Fig. 4.2).





**Figure 4.2** Shapes of different epithelial cells.

## CLASSIFICATION OF EPITHELIA

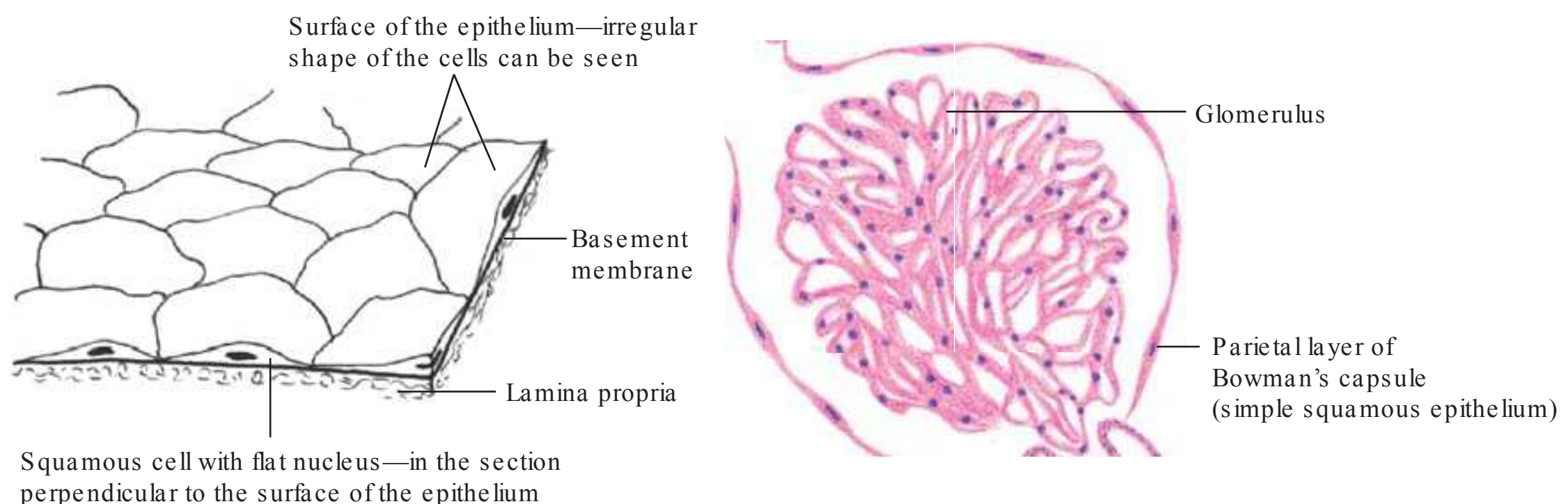
Classification of epithelia is based on the number of cell layers present.

- Simple epithelium has only one layer of cells.
- Stratified epithelium has two or more layers of cells.
- Pseudostratified epithelium has all its cells resting on the basement membrane, but not all the cells extend to the surface.

### Simple Epithelium

#### 1. Simple squamous epithelium

- It is composed of a single layer of flattened cells forming a continuous surface (Fig. 4.3).
- The nuclei of the cells are flattened.
- The apical surfaces of these cells (which can be seen on the surface of the epithelium) are irregular in shape (Fig. 4.3, left); however, they appear flat in the section passing perpendicular to the surface of the epithelium. The individual cell of the simple squamous epithelium can be compared with a 'half-fried egg,' with the yellow yolk representing the nucleus and the surrounding egg white representing the cytoplasm of the cell. When viewed from the top, the half-fried egg appears irregular in



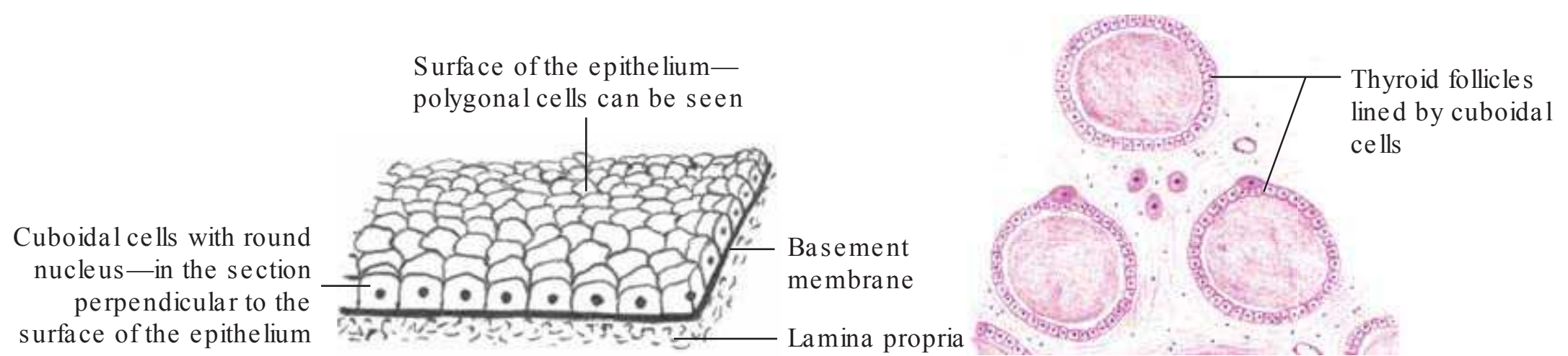
**Figure 4.3** Simple squamous epithelium. Example, right: Parietal layer of Bowman's capsule of renal corpuscle (H&E pencil drawing).

shape and the yolk appears circular, but if it is cut perpendicular to the surface in the centre, both the egg white and yellow yolk appear flat on the cut surface.

- Functions: Since the squamous epithelium comprises a single layer of thin cells, small molecules can easily pass through it (diffusion and filtration). However, it offers almost no protection.
- Examples: It lines the blood vessels (endothelium); body cavities such as pleural, pericardial and peritoneal cavities (mesothelium); and parietal layer of Bowman's capsule (renal corpuscle in kidney) (Fig. 4.3, right).

## 2. Simple cuboidal epithelium

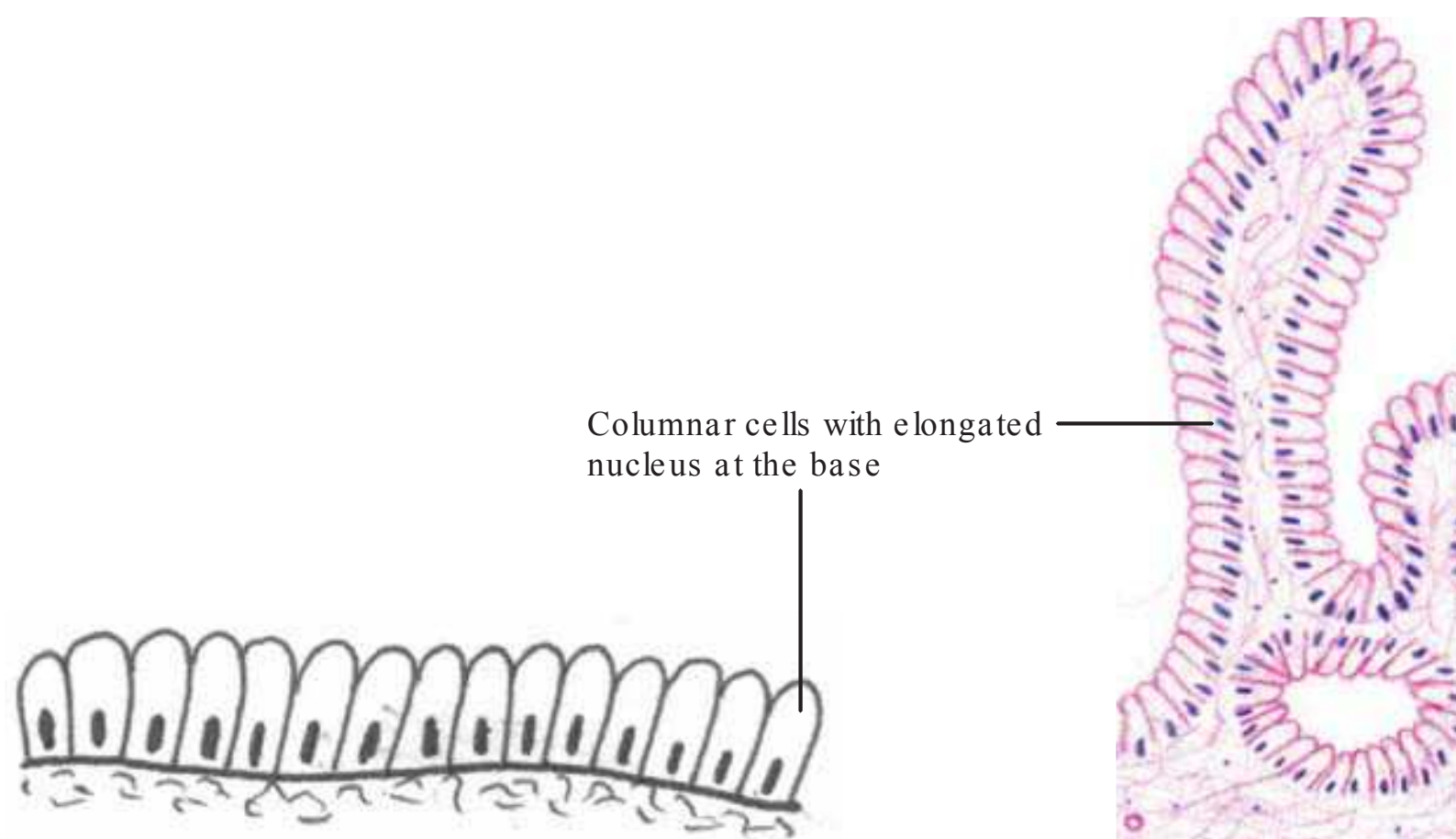
- On the surface of the epithelium the cells are polygonal in shape. They appear square shaped in the section drawn perpendicular to the surface of the epithelium.
- Nucleus of each cell is round and centrally placed (Fig. 4.4, left).
- Functions: The main functions are secretion, absorption and excretion. It offers some protection against toxic substances, mechanical injury, invasion of microorganisms and excessive water loss.
- Examples: It is present in thyroid follicles (Fig. 4.4, right), small ducts of glands, tubules of the kidney and surface of the ovaries.



**Figure 4.4** Simple cuboidal epithelium. Example, right: Thyroid follicles of the thyroid gland (H&E pencil drawing).

## 3. Simple columnar epithelium

- The height of cells is greater than their width.
- Nuclei are elongated and close to the base of the cells (Fig. 4.5, left).
- Functions: The main function of the simple columnar epithelium is secretion and absorption. It also acts as a barrier and offers some protection against toxic substances and invasion of microorganisms.
- Examples: It lines the internal surface of stomach, intestines, uterus and gallbladder (Fig. 4.5, right).



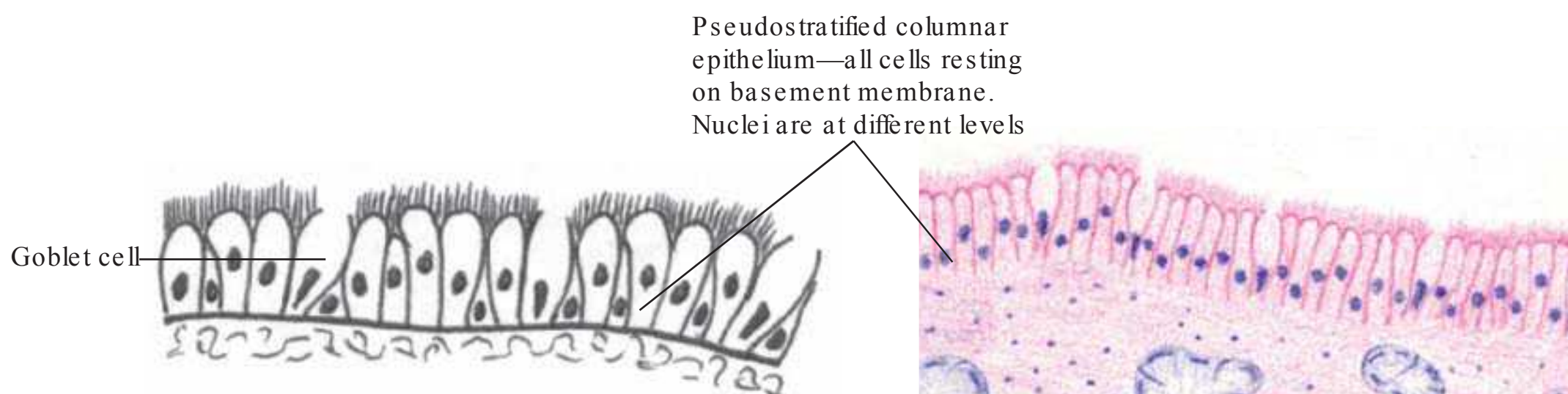
**Figure 4.5** Simple columnar epithelium. Example, right: Gallbladder mucosa (H&E pencil drawing).



## Pseudostratified Epithelium

### Pseudostratified columnar epithelium

- As mentioned earlier, in this type of epithelium, all cells rest on the basement membrane but only some of them reach the surface.
- Since the cells are of different heights, their nuclei are at different levels. This gives a false impression that the epithelium consists of two or more layers (Fig. 4.6, left).
- The larger airways of the respiratory tract are lined by ciliated pseudostratified columnar epithelium; the apical surface of the cells has cilia. Since this epithelium (ciliated pseudostratified columnar epithelium) is confined to the respiratory tract, it is also known as respiratory epithelium.
- Pseudostratified columnar epithelium is also present in certain parts of the male reproductive system. In these parts the apical surface of the cells has stereocilia which help in absorption. (It should be noted that the epithelium of large airways of the respiratory tract is pseudostratified columnar epithelium with goblet cells, whereas the same epithelium in parts of the male reproductive system is devoid of goblet cells.)
- Functions: In respiratory tract, functions of pseudostratified columnar epithelium are secretion of mucus and airway protection. The mucus covers the surface of the epithelium. Foreign particles present in the air get trapped in the mucus secreted by the epithelial cells; the cilia of the epithelial cells propel the mucus towards the oropharynx. It is then either coughed out or swallowed. In male reproductive system, absorption is the main function.
- Examples: It lines the larger airways of respiratory tract (Fig. 4.6, right).



**Figure 4.6** Ciliated pseudostratified columnar epithelium. Example, right: Respiratory epithelium of trachea (H&E pencil drawing).

## Stratified Epithelium

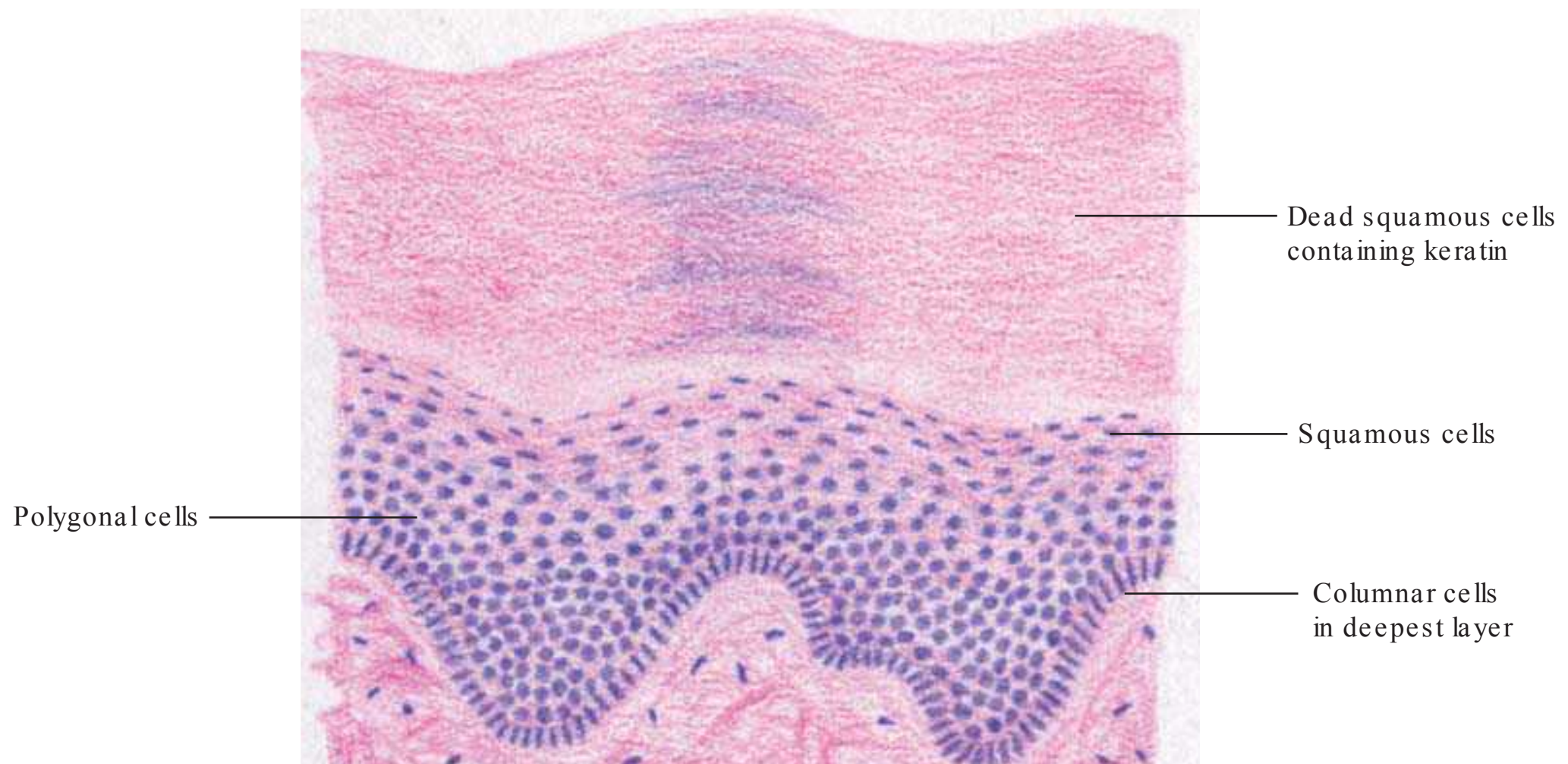
Stratified epithelia contain two or more layers of cells. They are further classified on the basis of the shape of the cells in the topmost layer. Cells in the deeper layers have different shapes.

### 1. Stratified squamous epithelium

It occurs in two forms—keratinised and non-keratinised.

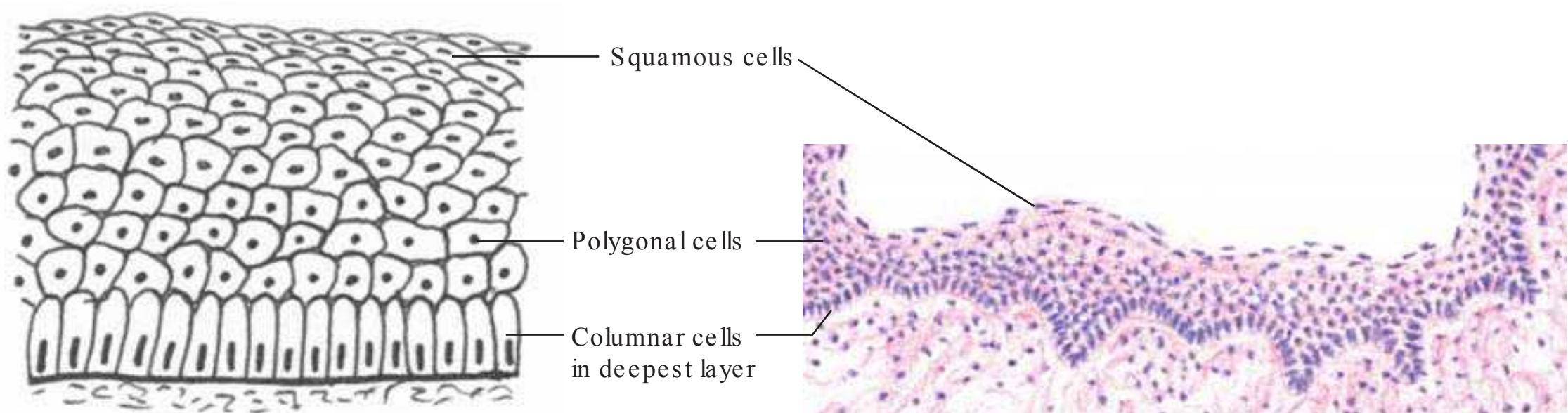
- Keratinised stratified squamous epithelium
  - Cells in the deepest layer are columnar or cuboidal; the cells superficial to this layer are polygonal in shape.
  - These polygonal cells gradually flatten in superficial layers and their nuclei become flat.
  - Near the surface of the epithelium, cells are keratinised and make the surface dry. These cells are dead and flat in shape, without a nucleus.
  - Functions: This epithelium acts as a barrier against infection, provides protection against mechanical injury and prevents excessive water loss.
  - Example: It is present in skin (which is a dry surface) (Fig. 4.7).





**Figure 4.7** Section of epidermis of the skin showing keratinised stratified squamous epithelium (H&E pencil drawing).

- Non-keratinised stratified squamous epithelium
  - This is structurally similar to keratinised stratified squamous epithelium, but its thickness is less and it does not have a superficial layer of dead cells (Fig. 4.8, left).
  - Function: It acts as a barrier and provides protection against mechanical injuries.
  - Examples: It lines wet surfaces such as oral cavity, oesophagus (Fig. 4.8, right), vagina, anal canal and vocal folds.



**Figure 4.8** Non-keratinised stratified squamous epithelium. Example, right: Oesophagus (H&E pencil drawing).

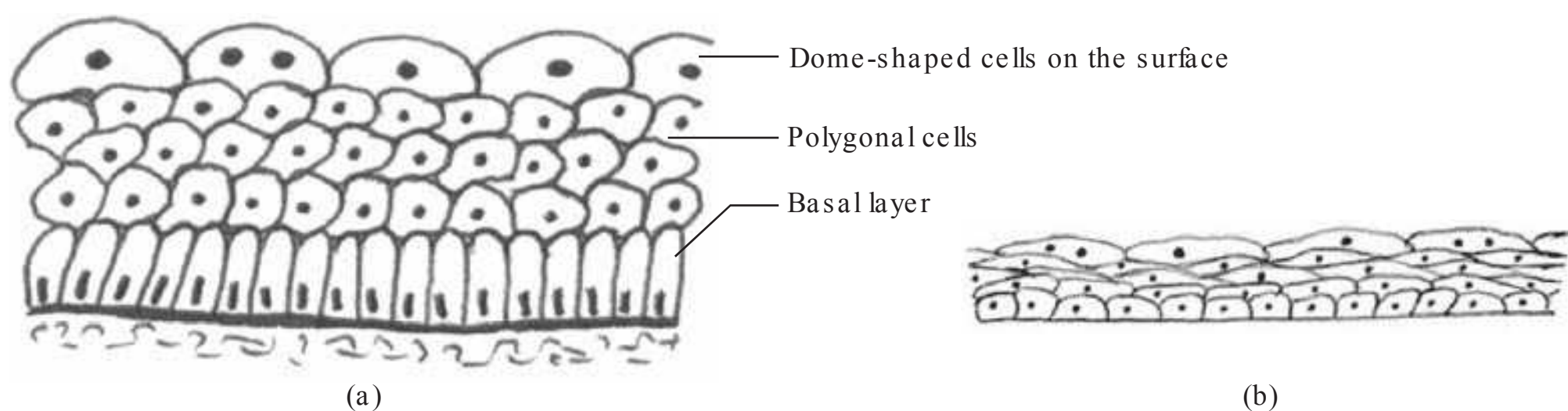
## 2. Stratified cuboidal and columnar epithelia

- Two-layered cuboidal epithelium is seen in the ducts of some glands such as sweat and salivary glands.
- Two-layered columnar epithelium is seen in larger ducts of some glands and conjunctiva.
- Both stratified cuboidal and columnar epithelia provide slightly higher level of protection than the simple epithelium, and they also act as a barrier.

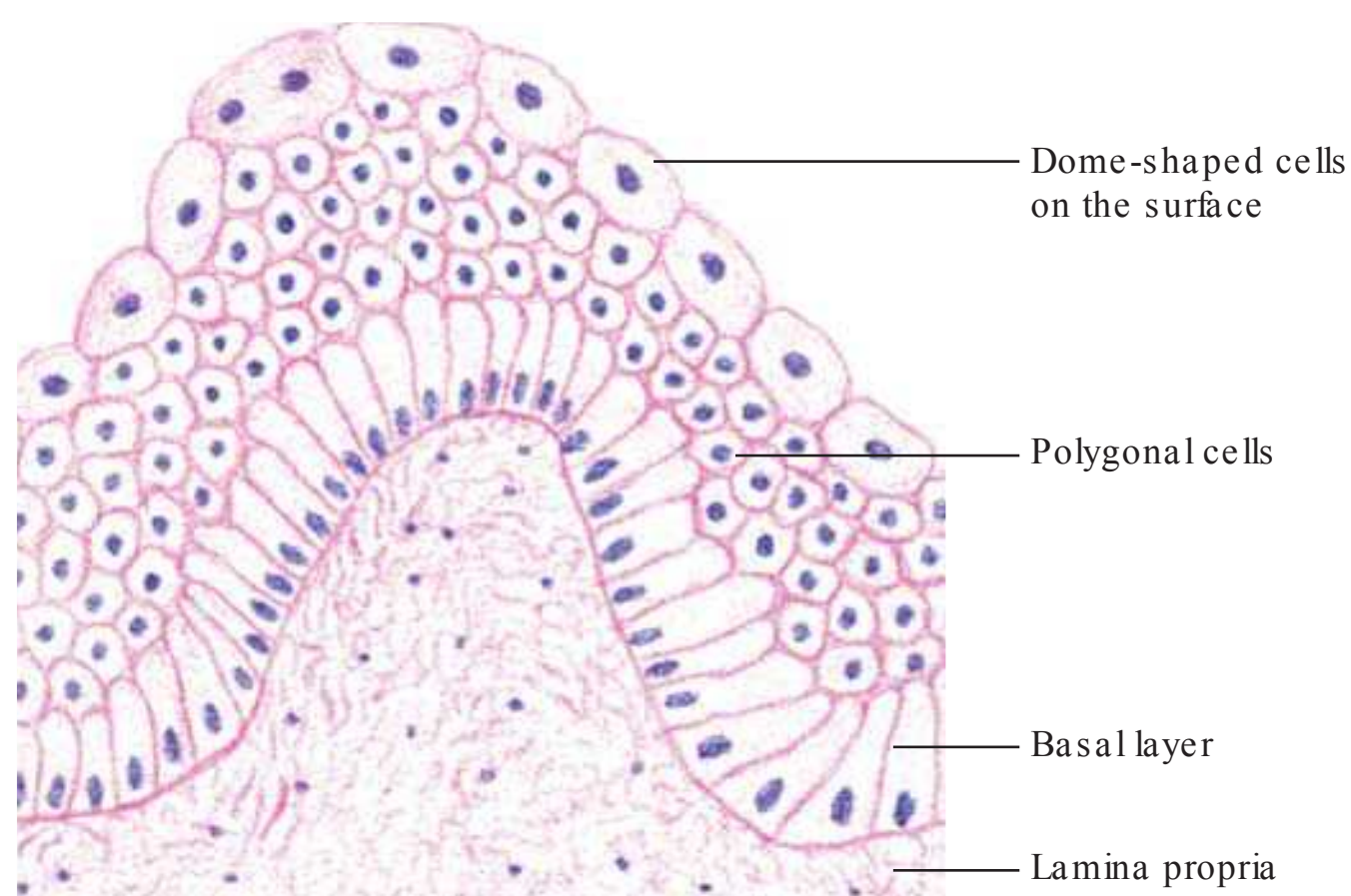
## 3. Transitional epithelium (Figs 4.9 and 4.10)

- It is a stratified epithelium, with capacity to stretch.
- It lines most of the urinary passage (urinary bladder, ureter, etc.); hence, it is also called urothelium.
- Basal cells are cuboidal to columnar.
- Cells superficial to the basal cells are polygonal.
- On the surface, cells are large and dome shaped; some of the surface cells may have two nuclei.





**Figure 4.9** Transitional epithelium in (a) relaxed state and (b) stretched state.



**Figure 4.10** Ureteric mucosa showing transitional epithelium (H&E pencil drawing).

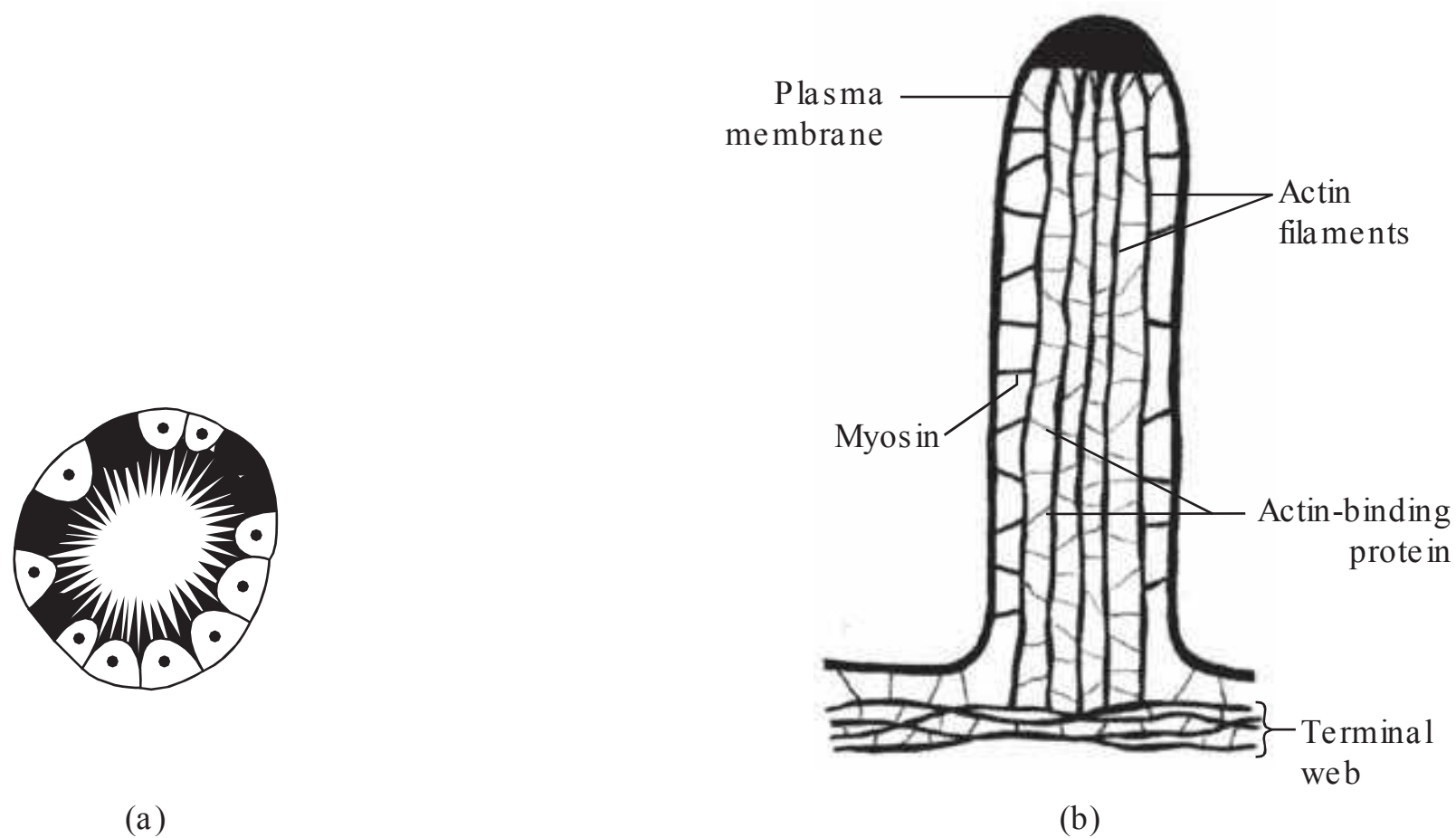
- Transitional epithelium has the ability to stretch. In relaxed state it is five to six layers thick; in stretched state the cells become flat and the epithelium appears to be two to three layers thick. This change in the shape of the cells allows the epithelium to stretch.

### SURFACE SPECIALISATIONS OF THE EPITHELIAL CELLS

Epithelial cells show some specialised structures on their surfaces for specific functions. On apical surface, these structures include microvilli, stereocilia, villi and flagellae. On lateral and basal surfaces, the structures present are junctional complexes.

#### **Microvilli (Singular: Microvillus)**

- These are finger-shaped extensions arising from the apical surface of the epithelial cells.
- Their main function is to increase the surface area of epithelial cells. They are found in epithelia specialised for absorption, for example, small intestine.
- Microvilli of the epithelial cells collectively form brush border or striated border on the surface of the epithelium (Fig. 4.11a).
- Each microvillus is supported by a core of actin filaments. These actin filaments are cross-linked by actin-binding proteins. The actin filaments are bound to the plasma membrane by the protein myosin. At the base of the microvillus, the actin filaments are attached to the terminal web. The terminal web is a horizontal meshwork of actin filaments located at the apical cytoplasm of the cell (Fig. 4.11b).



**Figure 4.11** (a) Transverse section of proximal convoluted tubule of kidney showing microvilli which form striated border. (b) Ultrastructure of a microvillus.

### Stereocilia

- These are extremely long microvilli which appear like thread-shaped extensions from the epithelial cells.
- These are non-motile structures and they increase the surface area of a cell (microvilli are shorter and mobile).
- They are present on the epithelial cells of the epididymis (Fig. 17.8, page 257) and hair cells in the inner ear.

### Cilia (Singular: Cilium)

- These are elongated, motile evaginations from the cell surface.
- They have a central pair of microtubules surrounded by nine pairs of microtubules (9 + 2 arrangement). It is described in detail in Chapter 3.
- They propel the fluid present on the epithelial surface in a particular direction.
- They are present on the epithelial cells of larger airways of the respiratory tract, fallopian tube, etc.

### Flagella (Singular: Flagellum)

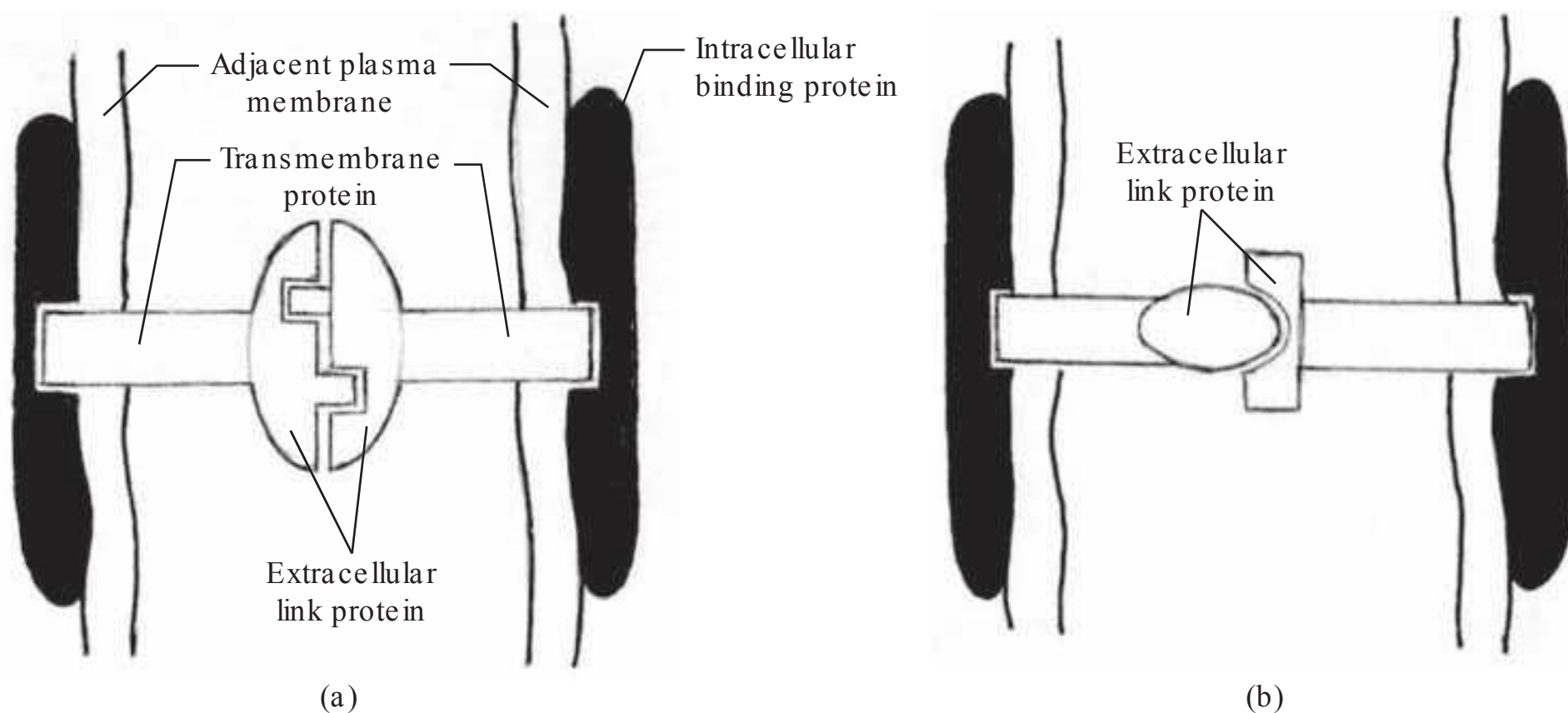
It is like a cilium, but it is longer. A cell has usually one or two flagellae. In humans, spermatozoa are the only cells which bear flagella.

### JUNCTIONAL COMPLEXES

The epithelial cells are tightly attached to each other or to extracellular matrix (described in Chapter 5) by specialised junctions.

- There are several types of cell adhesion molecules (CAMs), which are membrane proteins, responsible for these specialised junctions.
- These proteins consist of three domains (Fig. 4.12):
  - (a) Intracellular binding protein: It interacts with cytoskeleton and acts as an anchor within the cell.
  - (b) Transmembrane protein: It protrudes through the plasma membrane.
  - (c) Extracellular link protein: It binds with the other CAMs of same type (homophilic binding) or with different types of CAMs or extracellular matrix (heterophilic binding) (Fig. 4.12).





**Figure 4.12** Various domains of cell adhesion molecules (CAMs) in (a) homophilic binding and (b) heterophilic binding.

### Classification of CAMs

They are classified into two groups: (a) calcium dependent (this category CAMs require calcium) and (b) calcium independent (this group does not require calcium).

- Calcium-dependent CAMs
  - (a) Cadherins: They cause adhesion via homophilic binding. Three important types of cadherins are E-cadherins, in epithelia; P-cadherins, in placenta; and N-cadherins, in nervous tissue.
  - (b) Integrins: They are involved in binding of cells with components of the extracellular matrix (such as fibronectin).
  - (c) Selectins: They are present in leucocytes. They bind to carbohydrates present on other cell surfaces; however, the binding is relatively weak.
- Calcium-independent CAMs
 

There are two groups of calcium-independent CAMs:

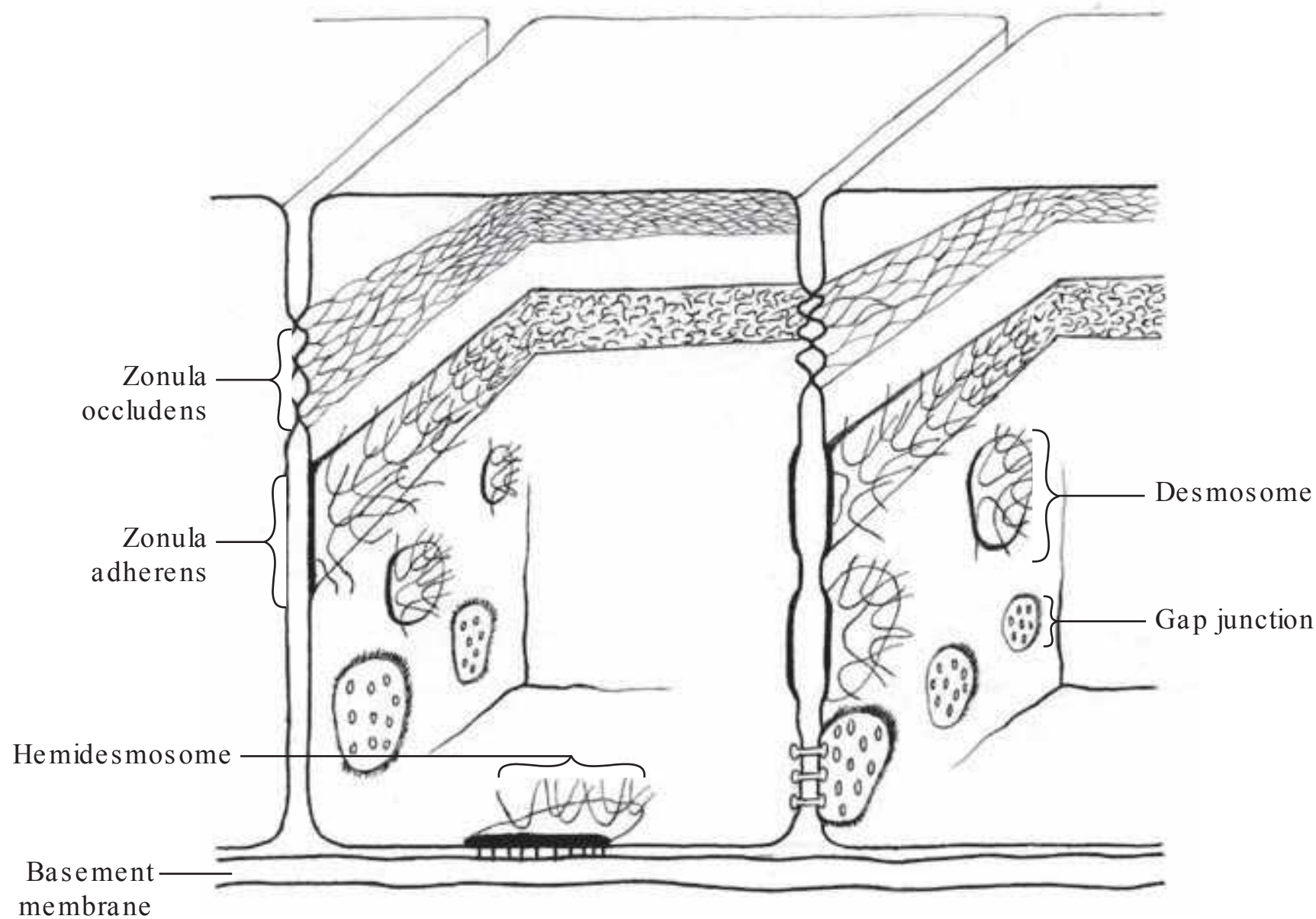
  - (a) NCAMs (neural cell adhesion molecules): Expressed by nerve cells
  - (b) ICAMs (intercellular cell adhesion molecules): Expressed by leucocytes

### Types of Junctions

Epithelial cells are tightly attached to each other by specialised junctions. These junctions are of three types: occluding, anchoring and gap junctions.

#### 1. Occluding junction (tight junction or zonula occludens)

- It is present just below the apical surface of the epithelial cell.
- It is formed by a network of sealing strands extending along the entire circumference of the cell (Fig. 4.13). These strands are composed of transmembrane proteins (CAMs) present on the plasma membrane.
- The outer layers of the plasma membrane of adjacent cells join with each other and obliterate the intercellular space between them (Fig. 4.14a).
- Functions
  - It binds the adjacent cells with each other.
  - It acts as a barrier as it prevents the movement of substances from the lumen of the viscera into the intercellular space. Certain substances enter the cell by diffusion or active transport and pass through the tissue. Thus, cells can control the movements of substances across the tissue.



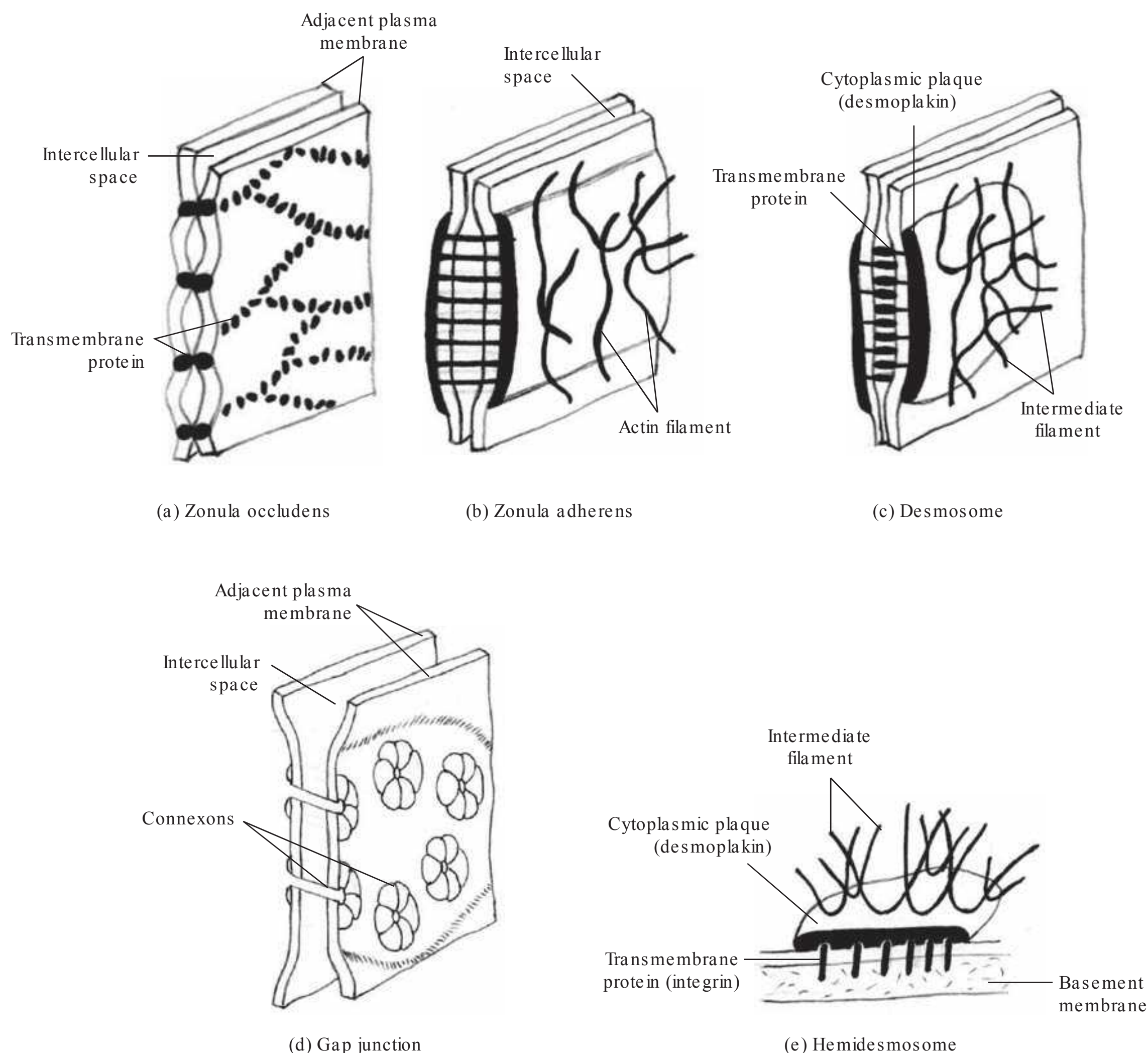
**Figure 4.13** Junctional complex. Zonula occludens are present below the apical surface of the cells. Zonula adherens and desmosomes are present below the zonula occludens. Hemidesmosomes bind the cell with basement membrane. Gap junctions facilitate communication between neighbouring cells.

- The apical surfaces of the cells have proteins (which are absent on other surfaces of the cell) performing specialised functions (such as receptor protein). The migration of these apical proteins to the other surfaces of the cell is prevented by tight junctions.

## 2. Anchoring (or adhesive) junction

- These junctions are most abundant in tissues that are subject to constant mechanical stress such as epidermis of the skin.
- They attach the cells (and their cytoskeletons) mechanically to their neighbouring cells or to the extracellular matrix.
- The anchoring junctions that bind the cells with each other are desmosomes and zonula adherens.
- The anchoring junction that binds the cells with the extracellular matrix is hemidesmosome.
- Desmosome (macula adherens)
  - Transmembrane protein (cadherin) is the actual anchor (Table 4.1).
  - The extracellular part of the transmembrane protein extends through the plasma membrane and gets attached with a similar transmembrane protein of the adjacent cell (Figs 4.13 and 4.14c).
  - The intracellular part of the transmembrane protein binds to the cytoplasmic plaque (made of the protein desmoplakin).
  - Intermediate filaments are attached to the cytoplasmic plaque.
  - Desmosomes provide resistance against the shearing force between neighbouring epithelial cells. Hence, they are more abundant in epithelium subjected to mechanical stresses such as epidermis of the skin.
- Zonula adherens (adhesive belt)
  - These are present as a band below the zonula occludens and completely surround the cell (Fig. 4.13).





**Figure 4.14** Types of junctional complexes.

**Table 4.1** The Anchoring (or Adhesive) Junctions

Junction	Cytoskeleton	CAM	Binds the cell with
Desmosomes	Intermediate filaments	Cadherin	Neighbouring cells
Zonula adherens	Actin filaments	Cadherin	Neighbouring cells
Hemidesmosomes	Intermediate filaments	Integrins	Basement membrane

CAM, cell adhesion molecule.

- The transmembrane protein (cadherin) gets attached to the actin filaments of the cells (Fig. 4.14b; Table 4.1).
- The actin fibres are linked to transmembrane protein via actin-binding protein.
- A similar junction, the fascia adherens, occurs in the intercalated discs of the cardiac muscles.



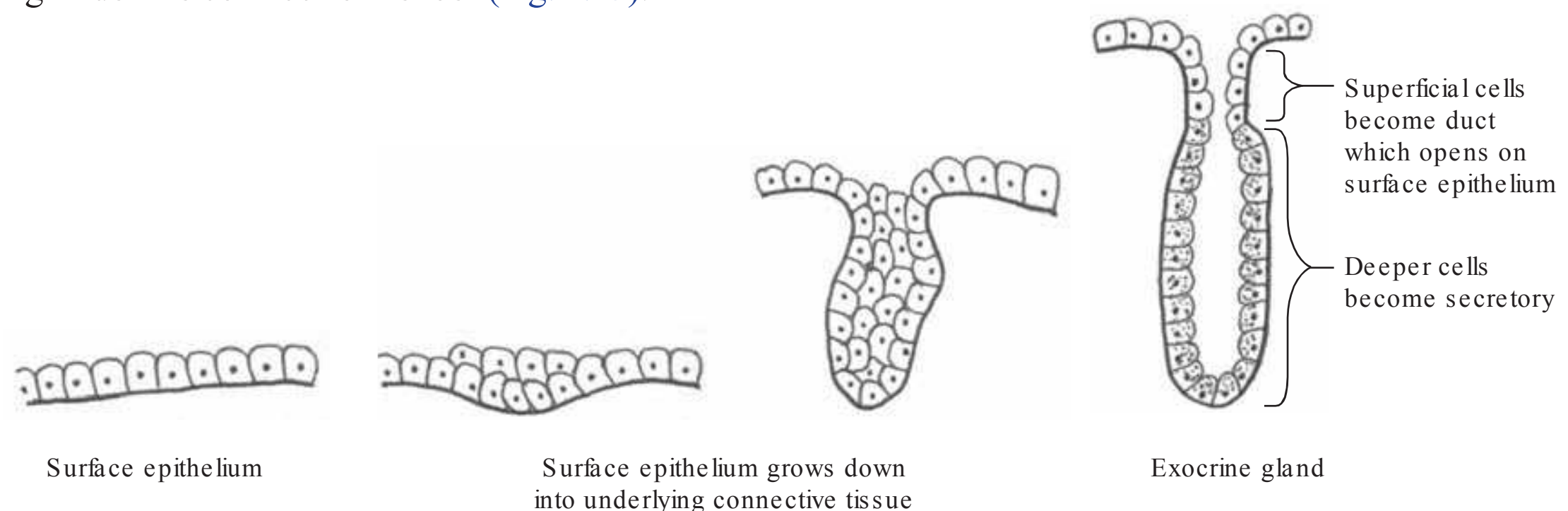
- Hemidesmosome
  - These anchoring junctions bind the basal surface of the cells with basement membrane (Fig. 4.13).
  - They resemble half of a desmosome (Fig. 4.14e).
  - In contrast to desmosomes, the transmembrane proteins in hemidesmosomes are integrins instead of cadherins (Table 4.1).
- Functions
  - The anchoring junction binds neighbouring cells. These attachments are stronger than occluding junctions.
  - It allows a group of cells to function as a cohesive unit.

### 3. Gap junction

- Gap junctions are important cell-to-cell contacts that facilitate communication between cells via electrical or metabolic coupling.
- They are less common in epithelia. They have an important role in the functioning of cardiac and smooth muscles where the signals can pass through these junctions from one cell to another. This results in the simultaneous recruitment of large numbers of contractile units during excitation.
- They are hexagonal intercellular channels called the connexons. They connect the plasma membrane of adjacent cells and allow the passage of ions and small molecules.
- The alignment of two connexons from adjacent cells across the gap between the two plasma membranes results in the complete intercellular gap junction channel (Figs 4.13 and 4.14d).
- Each connexon is formed by six copies of transmembrane proteins (Fig. 4.14d) called connexins.

## GLANDS

- Secretory cells derived from epithelia get organised along with supportive connective tissue to form a gland. The function of the glands is secretion.
- Glands can be exocrine or endocrine.
- Exocrine glands release their secretory product either through ducts or directly on the surface.
- Endocrine glands release the secretory product into the spaces between the glandular cells and from here the product diffuses into the bloodstream (see details in Chapter 20).
- Both endocrine and exocrine glands are developmentally derived from surface epithelium. The epithelial cells multiply and extend into the underlying connective tissue and form glands. The exocrine glands retain the connection with the surface epithelium through their ducts, whereas in endocrine glands this connection is lost (Fig. 4.15).



**Figure 4.15** Schematic diagram showing formation of glands from surface epithelium.

EXOCRINE GLANDS

Structurally exocrine glands may exist in a very simple form such as a single cell functioning as a gland and releasing its secretion on the surface. Alternately, they may also exist as multiple secretory cells (along with non-secretory supporting cells) which form a complex structure; the secretory product of such complex glands is conveyed by ducts which open on the surface.

Classification

All exocrine glands can be broadly classified into two groups, unicellular and multicellular glands.

Unicellular Glands

As the name suggests, these are glands consisting of single cells; the only example for this type of gland is a goblet cell, which secretes mucus. These cells release their products directly on the surface. Goblet cell is described in more detail later in the chapter.

Multicellular Glands

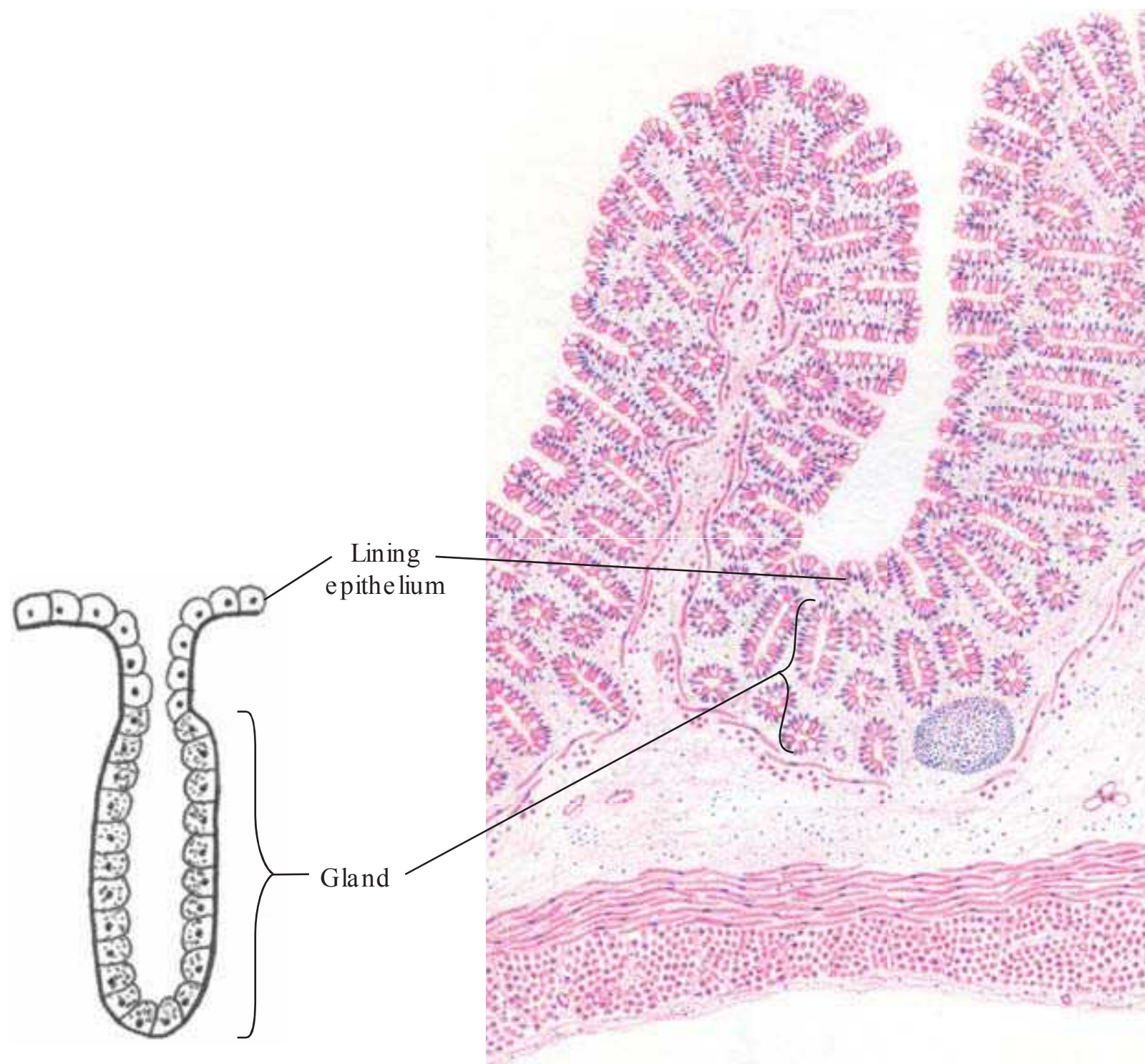
These glands consist of many secretory cells. Most of the exocrine glands are multicellular glands. They have ducts which convey their secretory product to the surface. They are further classified on the basis of the shape of their secretory part, the number of ducts draining the gland (Table 4.2), their secretory mechanisms and the secretory product itself.

Table 4.2 Classification of Multicellular Exocrine Glands on the Basis of the Shape of Secretory Unit and the Number of Ducts

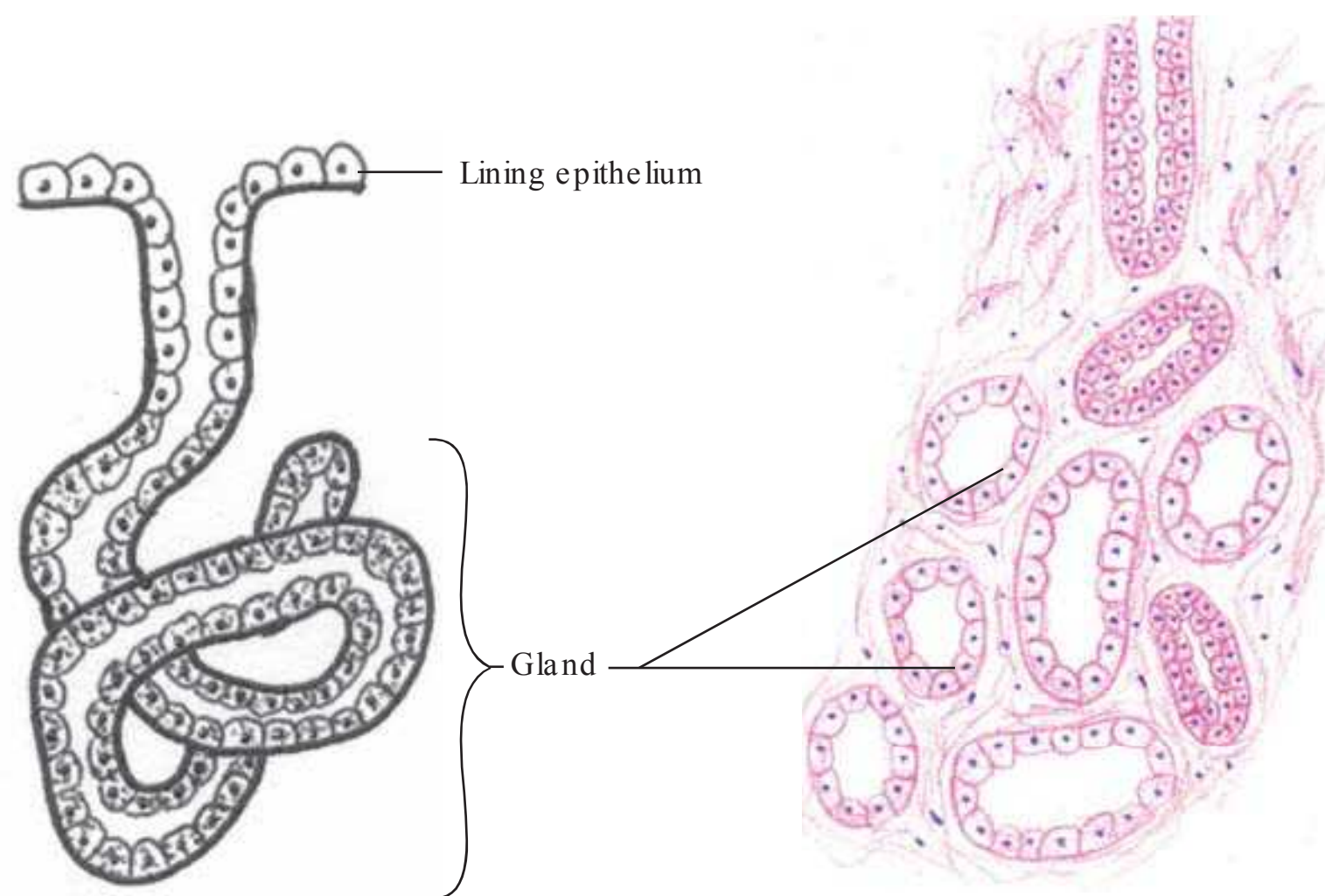
Type of gland	Secretory unit	Duct	Examples
Simple tubular	Tubular and straight	Unbranched	Intestinal glands (see Fig. 4.16)
Simple coiled tubular	Tubular and coiled	Unbranched	Sweat glands (see Fig. 4.17)
Simple branched tubular	Tubular and branched	Unbranched	Gastric glands (see Fig. 4.18)
Simple branched acinar	Acinar and branched	Unbranched	Sebaceous glands (see Fig. 4.19)
Compound tubular gland	Tubular	Branched	Brunner’s gland of duodenum (see Fig. 4.20)
Compound acinar	Acinar	Branched	Exocrine part of pancreas (see Fig. 4.21)
Compound tubuloacinar	Tubuloacinar	Branched	Submandibular salivary gland (see Fig. 4.22)

1. **On the basis of the shape of secretory unit**, multicellular exocrine glands can be tubular, acinar or alveolar. Combinations of these shapes also exist and these are called tubuloacinar glands. The secretory part can be straight, coiled or branched (Table 4.2).
  - Tubular gland: Secretory unit is tubular (like a tube) in shape (Figs 4.16–4.18).
  - Acinar gland: Secretory unit is round (Fig. 4.19).
  - Alveolar gland: Secretory unit is round and hollow.
2. **On the basis of number of ducts**, multicellular exocrine glands are either simple or compound.
  - Simple gland: Duct is unbranched. Secretory part can be tubular (simple tubular gland), acinar, coiled (simple coiled tubular gland) or branched (simple branched tubular gland) (Figs 4.16–4.19; Table 4.2).
  - Compound gland: Duct is branched. Secretory part can be of the same types as mentioned for simple gland (Figs 4.20–4.22; Table 4.2).
3. **On the basis of their secretory mechanisms**, multicellular exocrine glands can be merocrine, apocrine or holocrine.



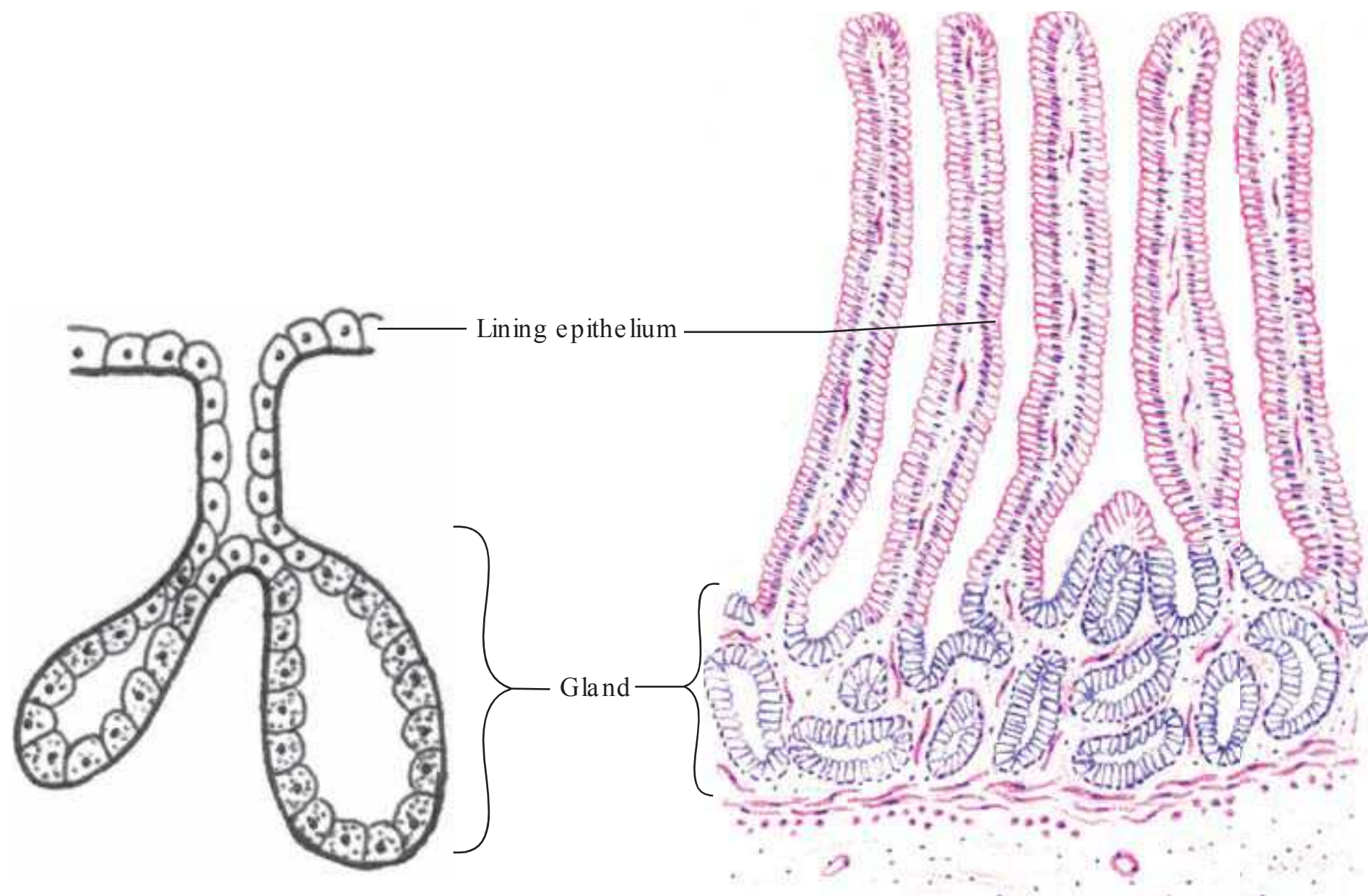


**Figure 4.16** Simple tubular gland—the duct is unbranched and secretory unit is tubular in shape. Example, right: Section of intestine showing intestinal glands (H&E pencil drawing).

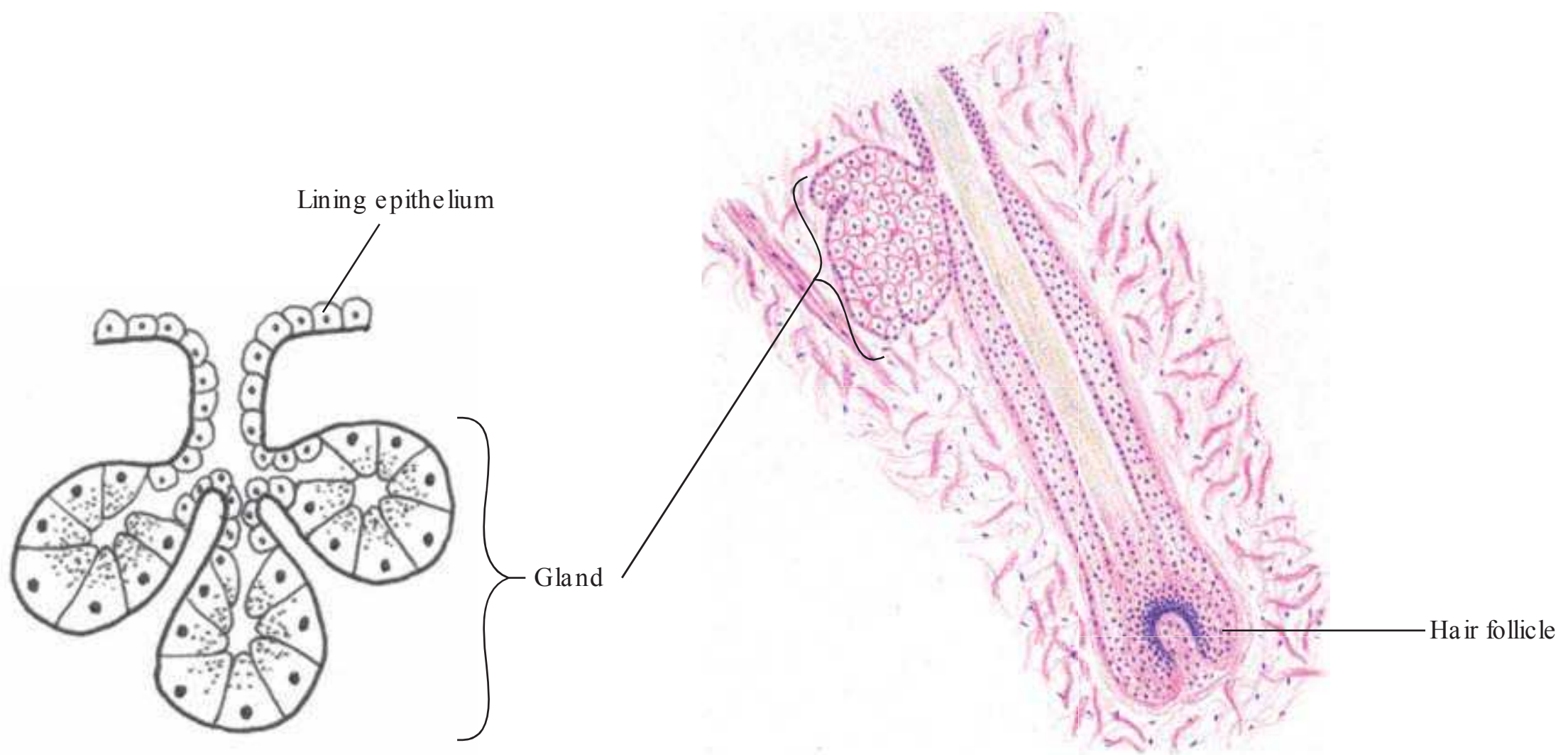


**Figure 4.17** Simple coiled tubular gland—the duct is unbranched and secretory unit is tubular in shape with coiling. Example, right: Section of skin showing sweat glands (H&E pencil drawing).





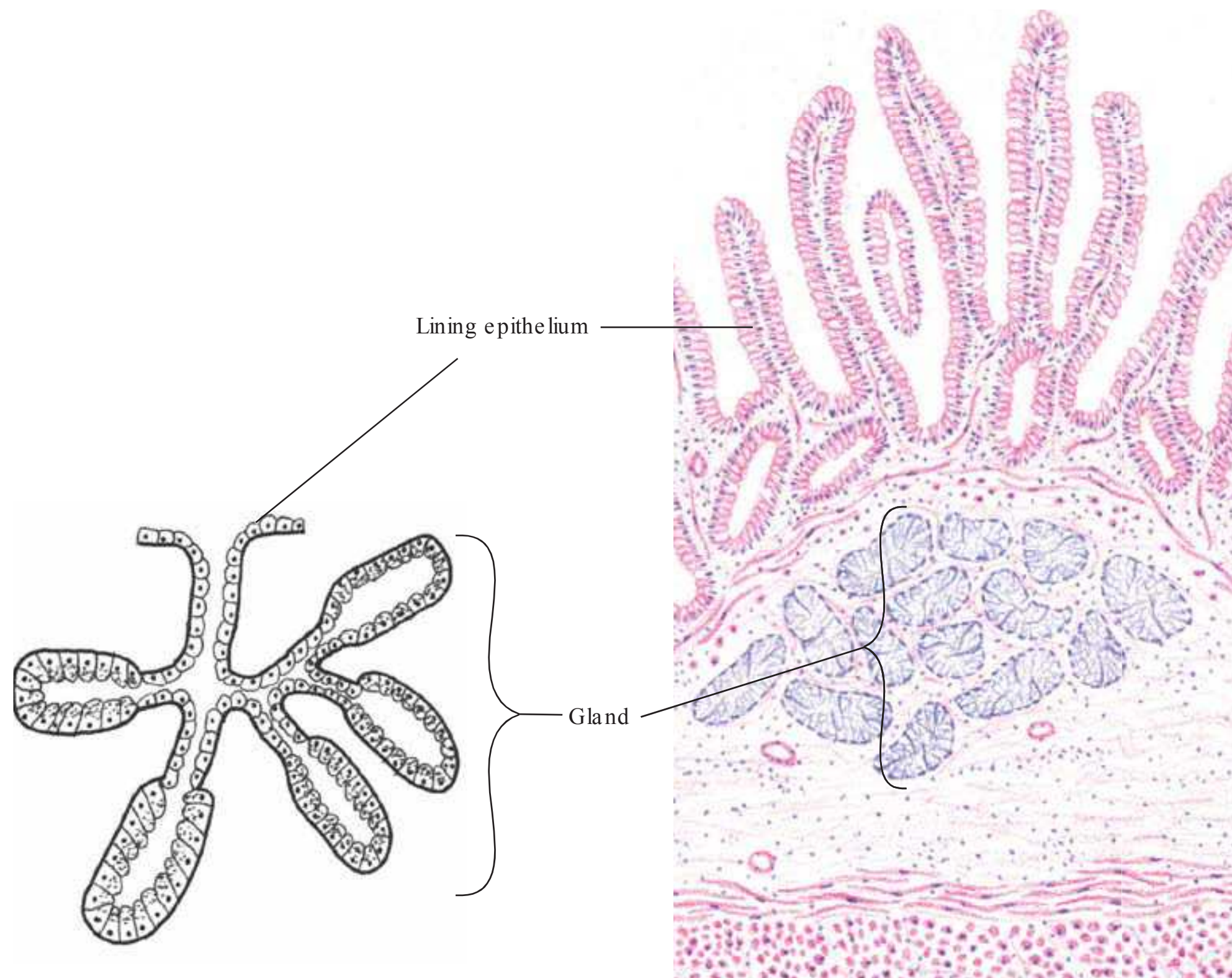
**Figure 4.18** Simple branched tubular gland—the duct is unbranched and secretory unit is tubular in shape and branched. Example, right: Section of stomach showing gastric glands (H&E pencil drawing).



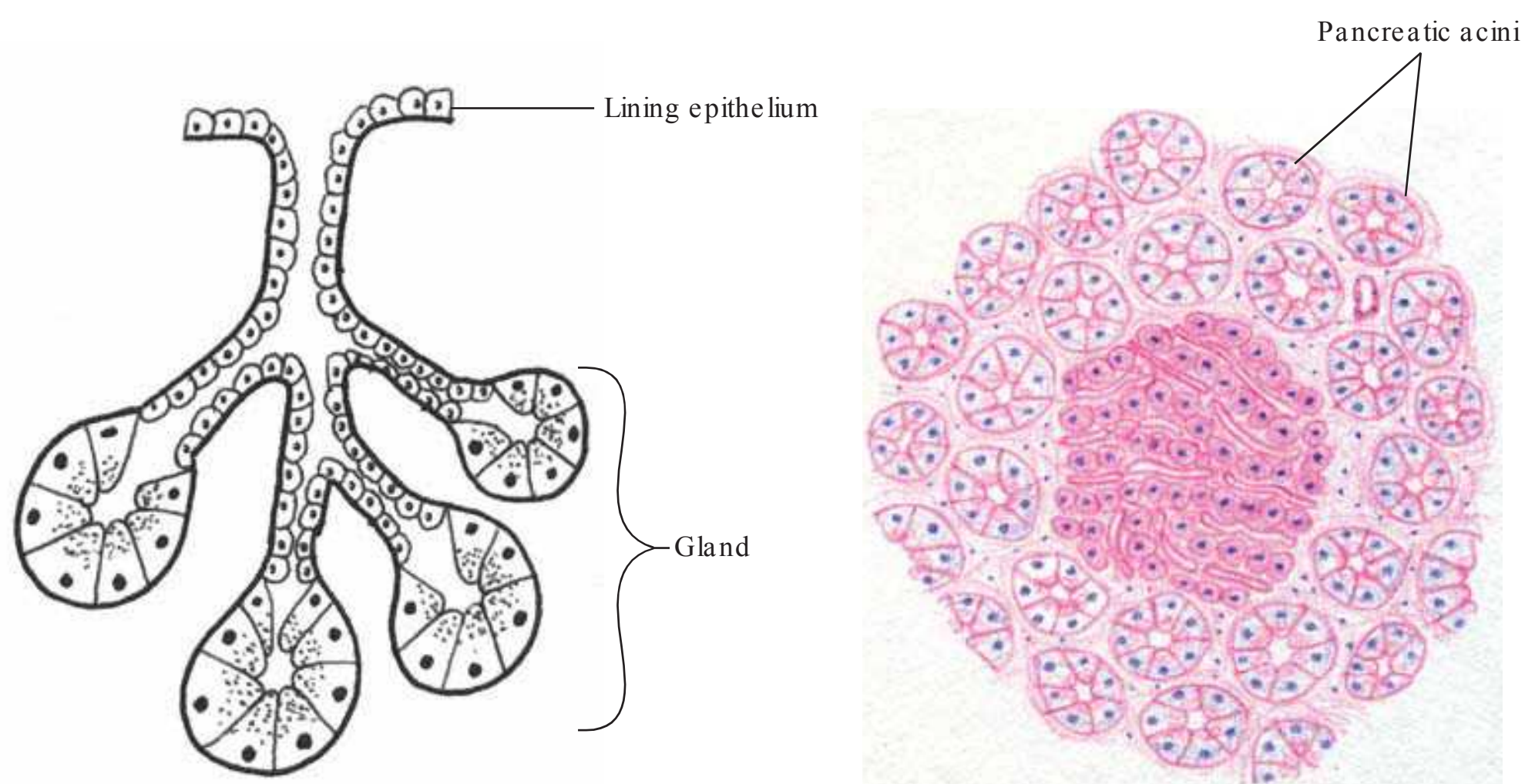
**Figure 4.19** Simple branched acinar gland—the duct is unbranched and secretory unit is acinar in shape and branched. Example, right: Section of skin showing sebaceous glands (H&E pencil drawing).

- Merocrine or eccrine gland: Secretory vesicles open onto the surface of the cell (Fig. 4.23a) and the secretory product is discharged (exocytosis) from the cell without any loss of cell substance, for example, acinar cells of pancreas and goblet cell.
- Apocrine gland: Part of the apical cytoplasm of the cells is lost along with the secretory product (Fig. 4.23b), for example, mammary glands and apocrine sweat glands.



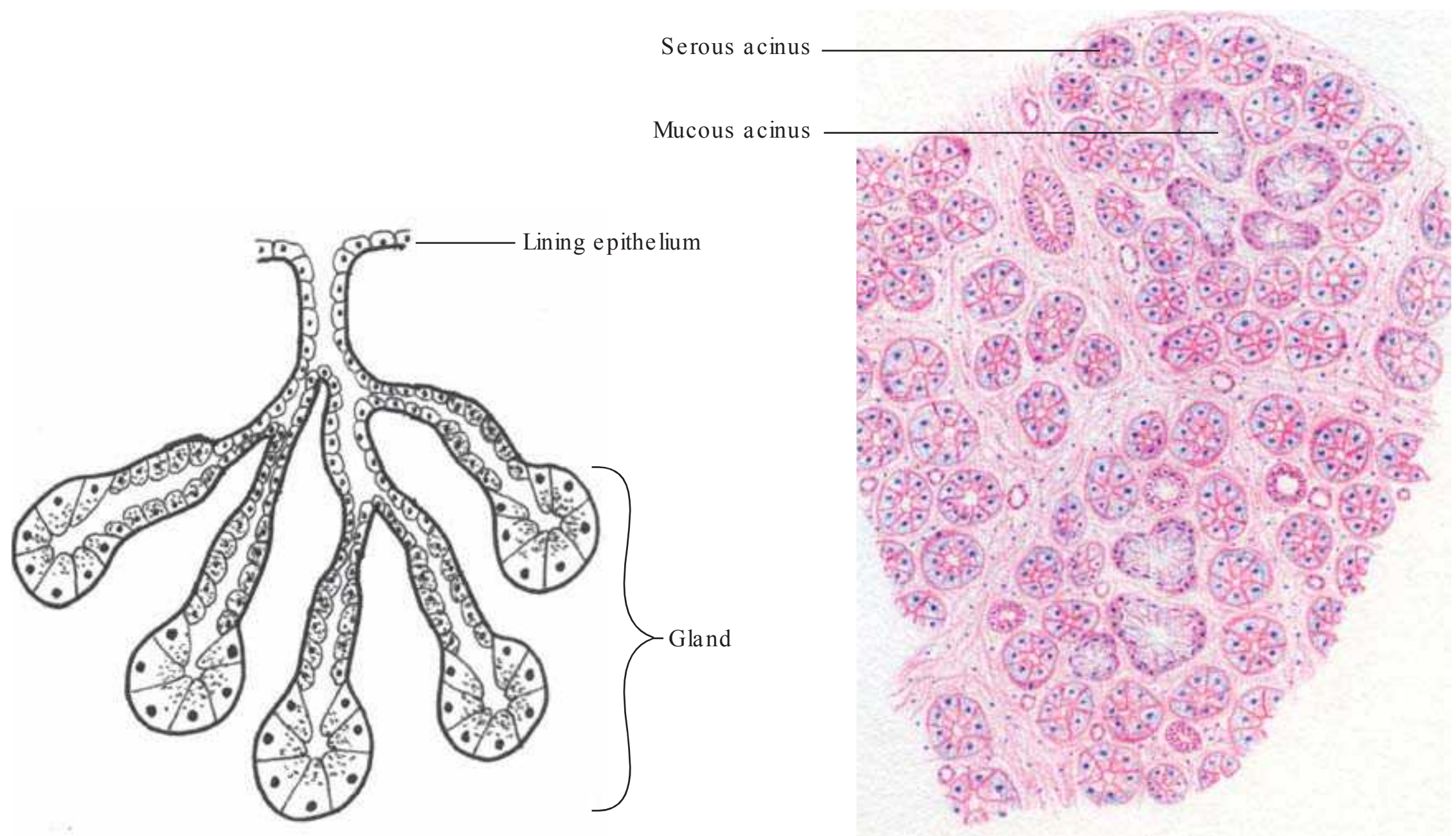


**Figure 4.20** Compound tubular gland—the duct is branched and secretory unit is tubular in shape. Example, right: Section of duodenum showing Brunner's glands (H&E pencil drawing).

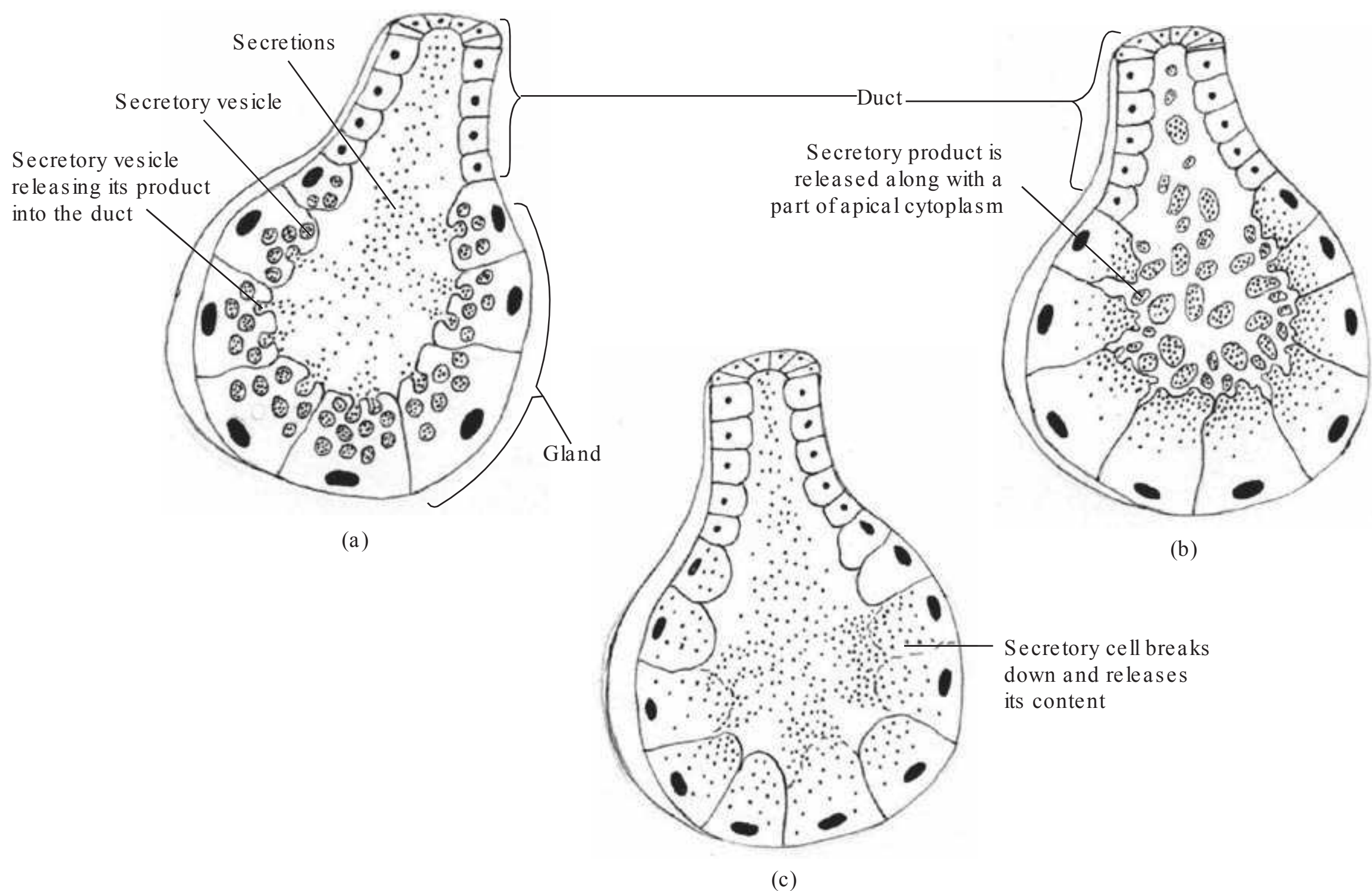


**Figure 4.21** Compound acinar gland—the duct is branched and secretory unit is acinar in shape. Example, right: Exocrine part of pancreas (H&E pencil drawing).





**Figure 4.22** Compound tubuloacinar gland—the duct is branched and secretory unit is tubuloacinar in shape. Example, right: Submandibular salivary gland (H&E pencil drawing).



**Figure 4.23** Different types of glands based on their secretory mechanisms. (a) Merocrine gland, (b) apocrine gland and (c) holocrine gland.



- Holocrine gland: The plasma membrane of the secretory cell breaks down and releases its secretion and the cell dies (Fig. 4.23c); however, the lost cell is replaced by a new cell, for example, sebaceous glands.

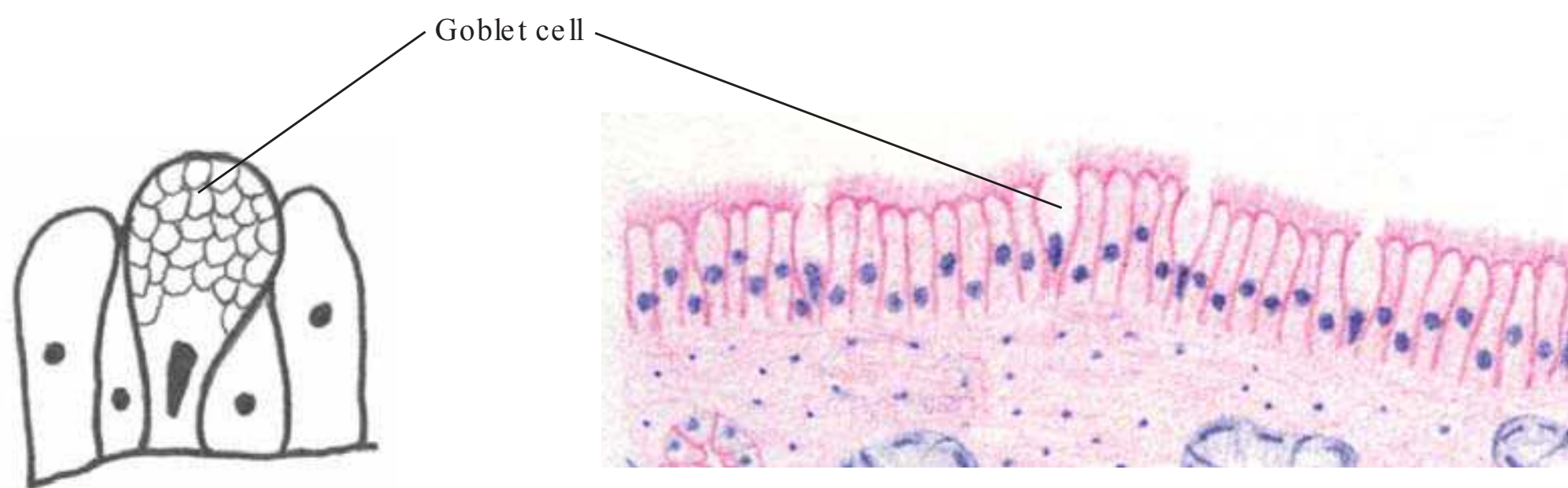
**4. On the basis of the nature of secretory product,** exocrine glands are classified into the following three groups:

- Serous
- Mucous
- Mixed

For more details, refer to Chapter 14.

### Goblet Cell

- It is a single secretory cell that occurs in the epithelium of many mucous membranes, for example, intestinal and respiratory mucosa.
- It secretes mucin.
- It rests on the basement membrane and has an elongated nucleus at the base (Fig. 4.24).
- The base of the cell is narrow and its upper portion is distended due to accumulation of the secretory product.



**Figure 4.24** Epithelium with goblet cell. Example, right: Section of respiratory epithelium showing goblet cells (H&E pencil drawing).

### Structural Organisation

All exocrine glands have basically three components: parenchyma, stroma and duct system (Fig. 4.25).

#### 1. Parenchyma

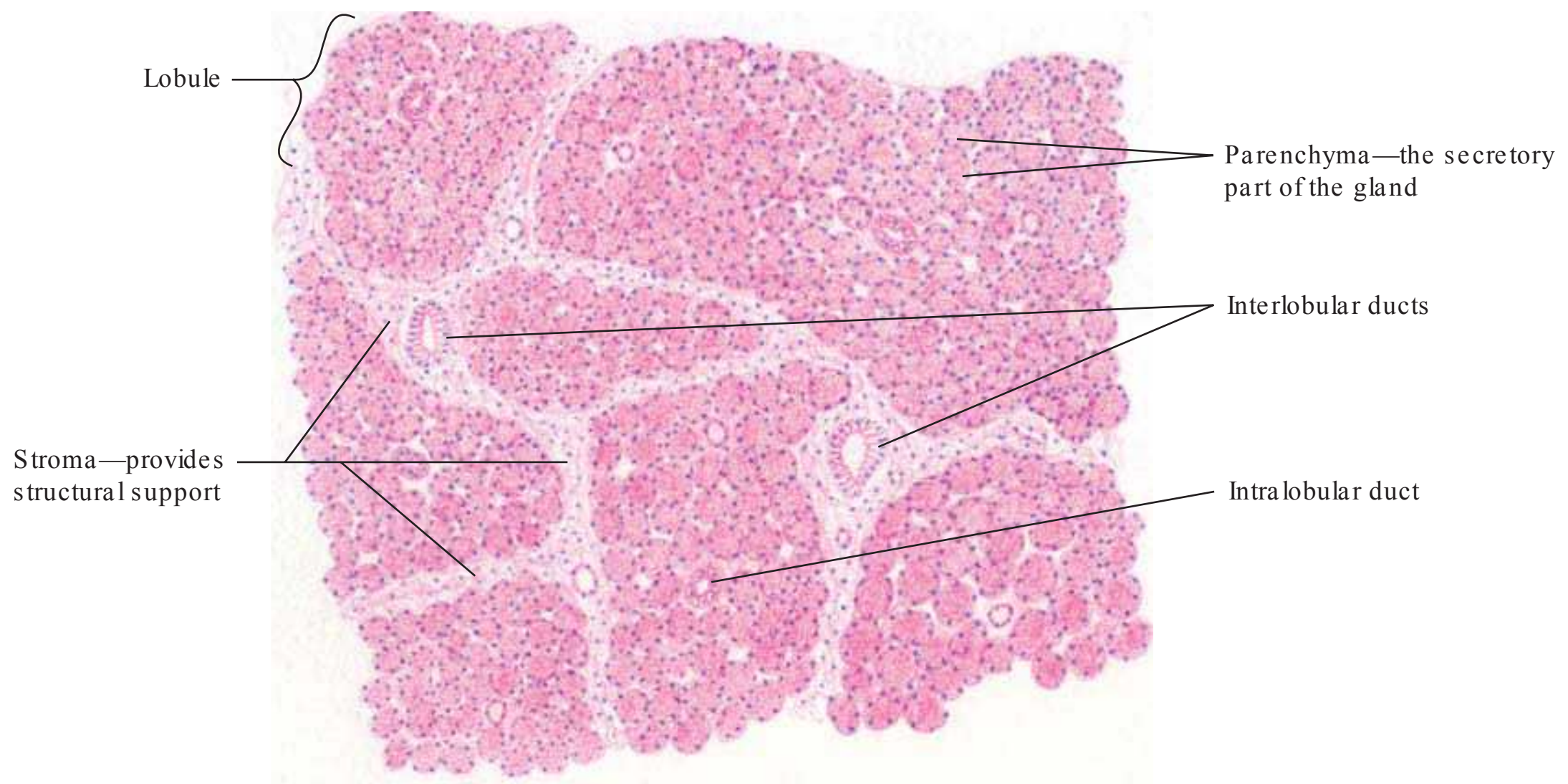
- It consists of cells responsible for the function (secretion) of the organ.

#### 2. Stroma

- It provides structural framework to the organ.
- It consists of connective tissue.
- A capsule may enclose the gland; numerous septa arising from the capsule may divide the parenchyma into lobes and lobules (small lobes) (Fig. 4.25).

#### 3. Duct system

- Duct system conveys the secretory product.
- Ducts within the lobule are called intralobular ducts (Fig. 4.25).
- Intralobular ducts drain into interlobular ducts (Fig. 4.25), which are the ducts present in the connective tissue separating the lobules.
- Interlobular ducts unite to form the main duct of the gland.



**Figure 4.25** Parotid gland—the three components of the gland can be seen (H&E pencil drawing).

- The secretory product is conveyed from intralobular ducts to interlobular ducts and finally to the main duct.

## CLINICAL CORRELATES

### Carcinoma

- Cancers of epithelial cell origin are called carcinomas. Cancers arising from squamous epithelium are called squamous cell carcinoma, while those arising from glandular epithelium are called adenocarcinoma.

### Metaplasia

- Reversible replacement of one adult cell type with another adult cell type is called metaplasia. It occurs due to chronic irritation. This transformation is not malignant but if the irritation of metaplastic epithelium continues it may become malignant. For example, cigarette smoke causes metaplasia in airways. The ciliated pseudostratified columnar epithelium is replaced by stratified squamous epithelium. If the irritation persists, it may turn malignant.

## KEYPOINTS

### Epithelium

#### Characteristics of Epithelium

- Highly cellular, with very little intercellular substance
- Avascular
- High regenerative capacity
- Rests on basement membrane
- Lines or covers the surfaces
- Forms exocrine and endocrine glands
- Is derived from all the three germ layers



Types of epithelium		Example
Simple—it has only one layer of cells	Squamous—flat cells with flat nucleus (Fig. 4.3)	Endothelium, mesothelium and parietal layer of Bowman’s capsule
	Cuboidal—cuboidal cells with round nucleus in the centre (Fig. 4.4)	Follicles of the thyroid gland and tubules of the kidney
	Columnar—tall cells with elongated nucleus near the base (Fig. 4.5)	Lining of the internal surface of stomach, intestines, uterus and gallbladder
Stratified—it has two or more layers of cells	Keratinised stratified squamous epithelium (Fig. 4.7)	Skin
	Non-keratinised stratified squamous epithelium (Fig. 4.8)	Lining of the wet surfaces such as oral cavity, oesophagus, vagina, anal canal and vocal folds
	Transitional epithelium (Fig. 4.10)	Lining of most of the urinary passage
Pseudostratified—single layer of cells but appears as multiple layers	Single layer of cells; nuclei are at different levels (Fig. 4.6)	Larger airways of respiratory tract

Exocrine Glands

Exocrine glands can be unicellular (e.g. goblet cell) (Fig. 4.24) or multicellular.

Classification of Multicellular Exocrine Glands

On the basis of the shape of the secretory unit (Figs 4.16–4.22)	<ul style="list-style-type: none"><li>• Tubular gland</li><li>• Acinar gland</li><li>• Alveolar gland</li></ul>
On the basis of the number of ducts draining the gland (Figs 4.16–4.22)	<ul style="list-style-type: none"><li>• Simple gland—duct is unbranched</li><li>• Compound gland—duct is branched</li></ul>
On the basis of the secretory mechanism (Fig. 4.23)	<ul style="list-style-type: none"><li>• Merocrine, e.g. goblet cell</li><li>• Apocrine, e.g. mammary glands</li><li>• Holocrine, e.g. sebaceous glands</li></ul>
On the basis of the nature of secretory products	<ul style="list-style-type: none"><li>• Serous</li><li>• Mucous</li><li>• Mixed</li></ul>

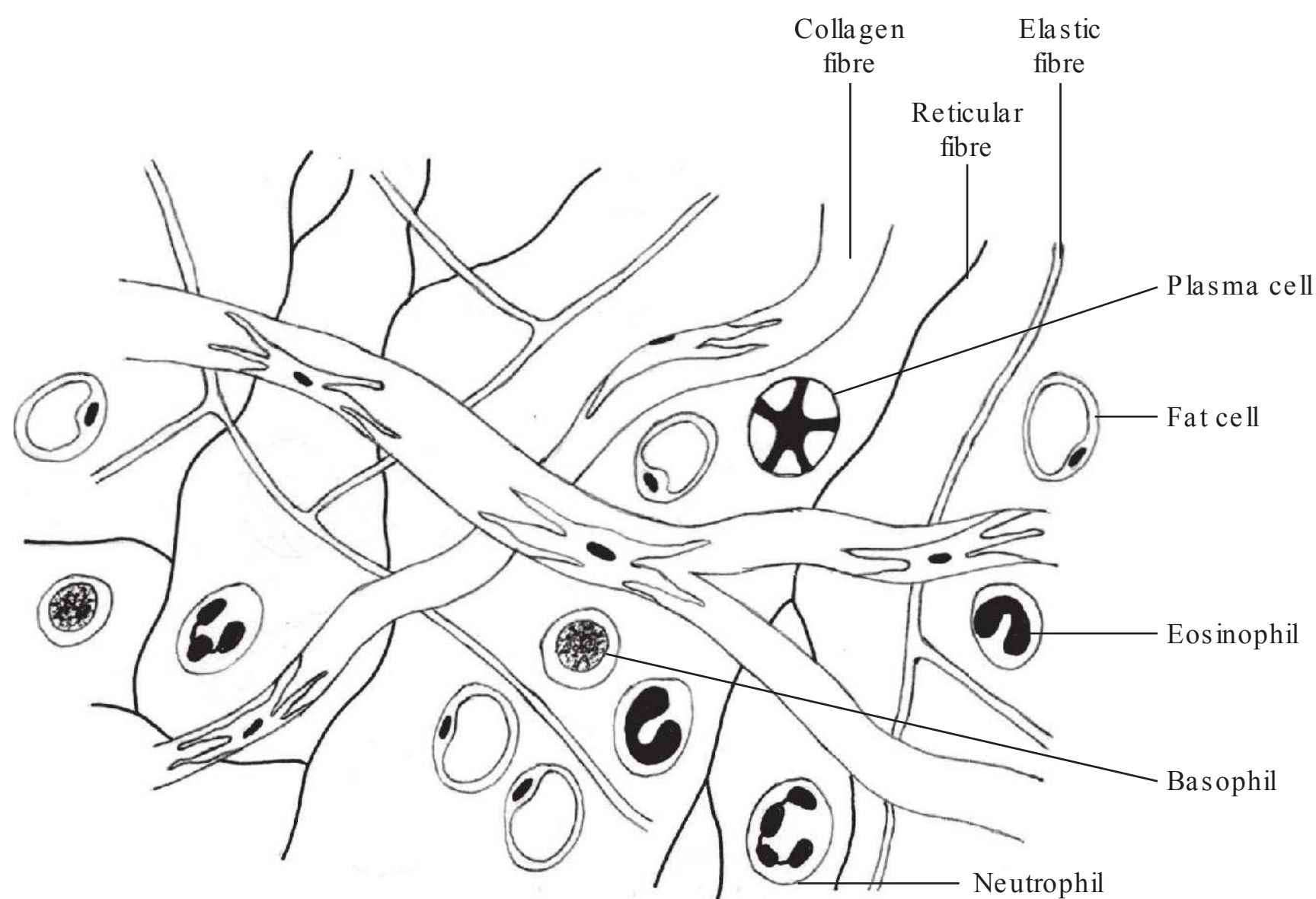
SELF-ASSESSMENT

1. What are the four basic tissues in the body?
2. Define epithelium. How does it get its nutrition?
3. What is mucosa?
4. What are the different types of epithelium? Give examples for each.
5. Compare microvilli, cilia, stereocilia and flagellae.
6. Classify the exocrine glands. Give examples for each.



# Connective Tissue

- Among the four basic tissues (epithelial, connective, muscle and nervous tissues), connective tissue is the most diverse, having a variety of functions. It is the most abundant tissue in the human body.
- Connective tissue consists of the following (Fig. 5.1):
  - (a) Cells: The various cells of the connective tissue have been described later in the chapter.
  - (b) Extracellular matrix: Extracellular matrix consists of ground substance and fibres.
- Though connective tissue is diverse and is present in different forms in the body (as discussed subsequently), the basic structural components of connective tissue remain the same.
- Connective tissue is derived from mesenchyme. The mesenchyme is derived from mesoderm in the entire body except in the head region, where it is derived from neural crest cells which are derivatives of ectoderm (refer Embryology textbooks for further details).



**Figure 5.1** Components of connective tissue. (Fibres are labelled at the top and cells are labelled on the right side of the diagram.)

- Functions: The major functions of connective tissue are as follows:
  - (a) It is present in between the cells, tissues and organs and binds them together and provides structural support to them.
  - (b) It is the tissue through which nutrients, oxygen and metabolites diffuse to and from the cells of the body.
  - (c) It provides immunological defence through its various cells.
  - (d) It also helps in wound healing and scar formation.
  - (e) It stores fat (in adipocytes).

## EXTRACELLULAR MATRIX

As mentioned earlier, the extracellular matrix consists of ground substance and fibres.

### GROUND SUBSTANCE

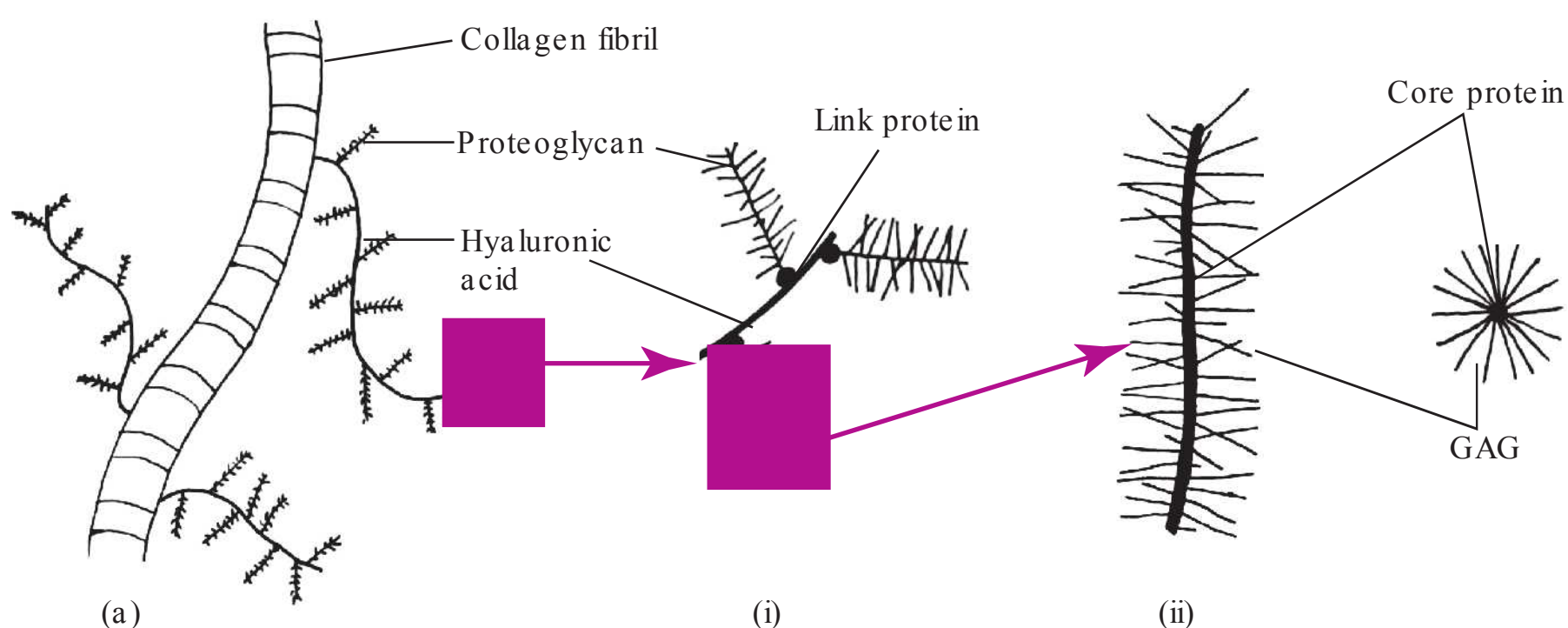
- It is a transparent, gel-like substance that is composed of glycosaminoglycans, proteoglycans and glycoproteins.
- It acts as a lubricant and is also a medium for the exchange of nutrients and metabolites between the cells of the connective tissue and blood. It also prevents the spread of microorganisms.
- Cells and fibres of the connective tissue are present in the ground substance.

### Glycosaminoglycans (GAGs)

- Glycosaminoglycans or mucopolysaccharides are long-chain unbranched polysaccharides.
- Glycosaminoglycans are negatively charged; they attract osmotically active cations such as sodium ions and make the matrix a hydrated gel through which water, oxygen and solutes pass through to get to the cells.
- Based on their chemical structure, different types of GAGs are present. These are hyaluronic acid, chondroitin sulphate, dermatan sulphate, heparin and heparan sulphate and keratan sulphate.

### Proteoglycans

- These are large molecules consisting of a core protein to which numerous GAGs are attached (Fig. 5.2). However, amongst the different GAGs, hyaluronic acid does not bind to the core protein, and hence it does not form proteoglycan.
- Core proteins of proteoglycans bind with long strand of hyaluronic acid through link proteins.



**Figure 5.2** Constituents of extracellular matrix. (a) Organisation of various extracellular molecules. Inset (i) shows binding of proteoglycans with hyaluronic acid through link protein. Inset (ii) shows proteoglycan molecule, which consists of core protein to which numerous glycosaminoglycans (GAGs) are attached.

## Glycoproteins

- These are proteins to which oligosaccharide chains are attached.
- They bring about adhesion between cells and extracellular matrix.
- There are several types of glycoproteins in the ground substance; some of these are as follows:
  - (a) Fibronectin: It is a multifunctional glycoprotein; it mediates the adhesion of cells to the extracellular matrix.
  - (b) Laminin: It mediates the adhesion of epithelial cells to basement membrane.
  - (c) Entactin: It is a link protein which binds laminin type IV collagen of basement membrane.
  - (d) Osteonectin: It is present in the bones and plays an important role in bone mineralisation.
  - (e) Chondronectin: It is present in cartilages; it mediates the adhesion of chondrocytes to the extracellular matrix.

## FIBRES

- Fibres are present in the ground substance of connective tissue.
- These are synthesised by fibroblasts.
- There are three types of fibres—collagen, elastic and reticular fibres.
- Collagen and reticular fibres are composed of collagen protein and elastic fibres are composed of elastin protein.

## Collagen Fibres

- These are present in almost all the connective tissues of the body and provide toughness and tensile strength to the tissue.
- An individual collagen fibre does not branch and is thick and wavy. This can be appreciated in [Figure 5.13](#). Collagen fibres are eosinophilic; in elastic Van Gieson stain preparation they appear red.
- Structurally, a collagen molecule (tropocollagen) consists of three polypeptide chains (α chains) wound around one another like a triple helix. Different types of α chains give rise to different types of collagen.
- There are more than a dozen varieties of collagen in the body. The most common forms are listed below:
  - (a) Type I collagen: Present in tendon, ligaments, dermis, fascia, etc.
  - (b) Type II collagen: Present in the hyaline cartilage.
  - (c) Type III collagen: Present in reticular fibres.
  - (d) Type IV collagen: Present in the basement membrane.

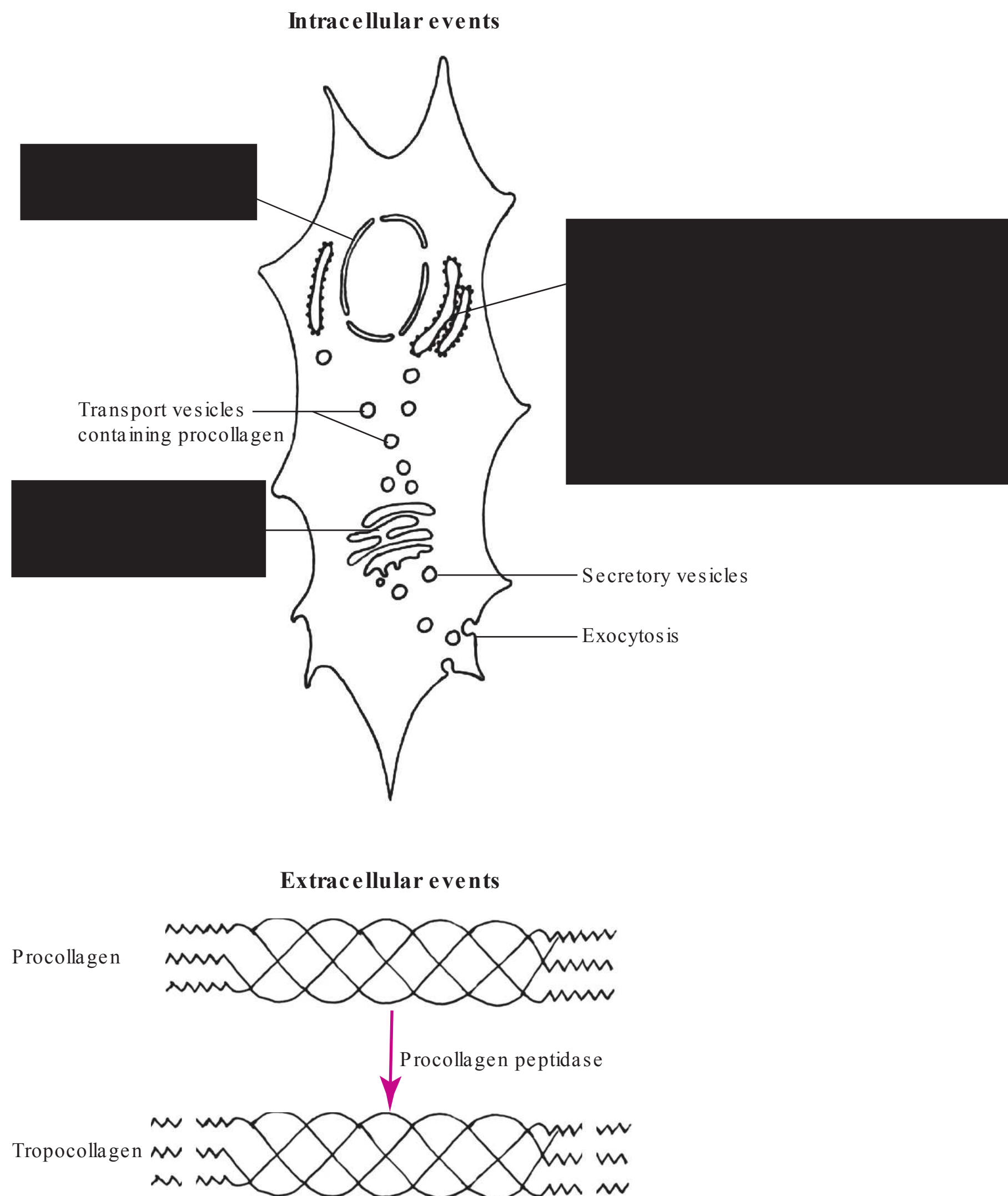
## Synthesis of Collagen Fibre

- Synthesis of collagen fibre involves several events, some within the cell (fibroblast) and some outside the cell.
- Procollagen, the precursor of collagen, is formed inside the fibroblast. Procollagen is then secreted into the extracellular matrix.



### Intracellular Events (Fig. 5.3)

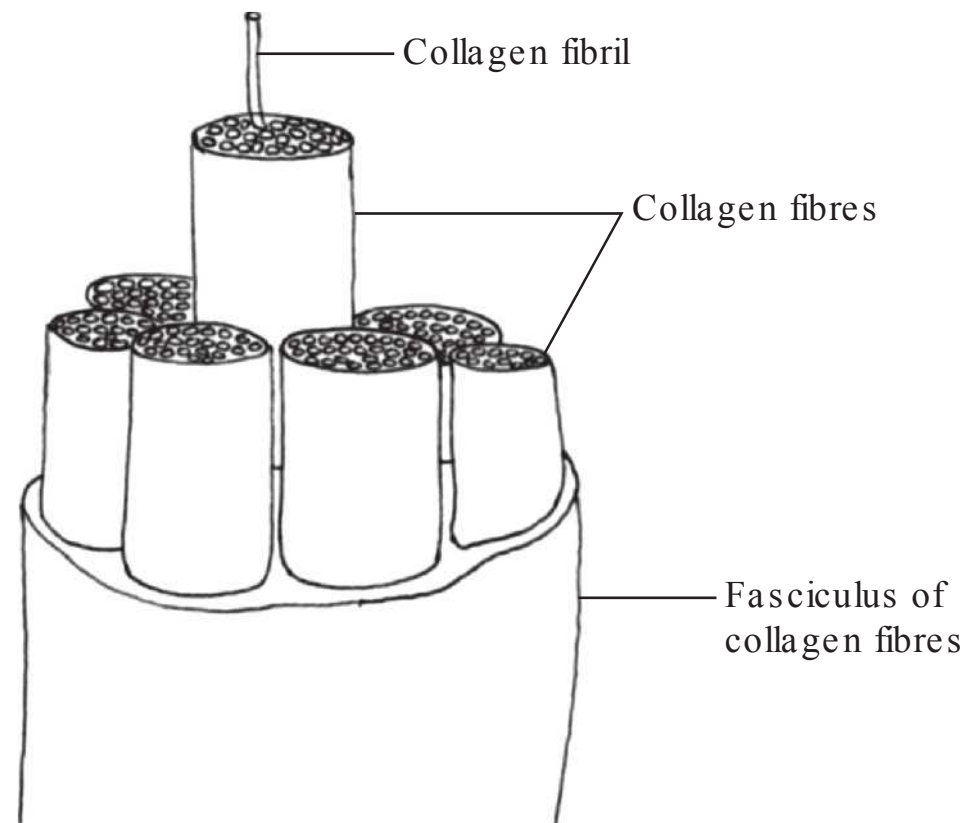
- Translation of mRNA in rough endoplasmic reticulum produces procollagen. Procollagen undergoes extensive posttranslational modification.
- Hydroxylation of proline and lysine residues of polypeptide chains occurs. This step requires vitamin C as a cofactor.
- Glycosylation (addition of sugar) of hydroxylysine residues occurs.
- Formation of procollagen: Three polypeptide chains coil around one another to form a triple helix—the procollagen.
- Procollagen is packed into secretory vesicle in Golgi complex and released from the secretory vesicle into the extracellular space by exocytosis.



**Figure 5.3** Steps of collagen fibril synthesis.

*Extracellular Events* (Fig. 5.3)

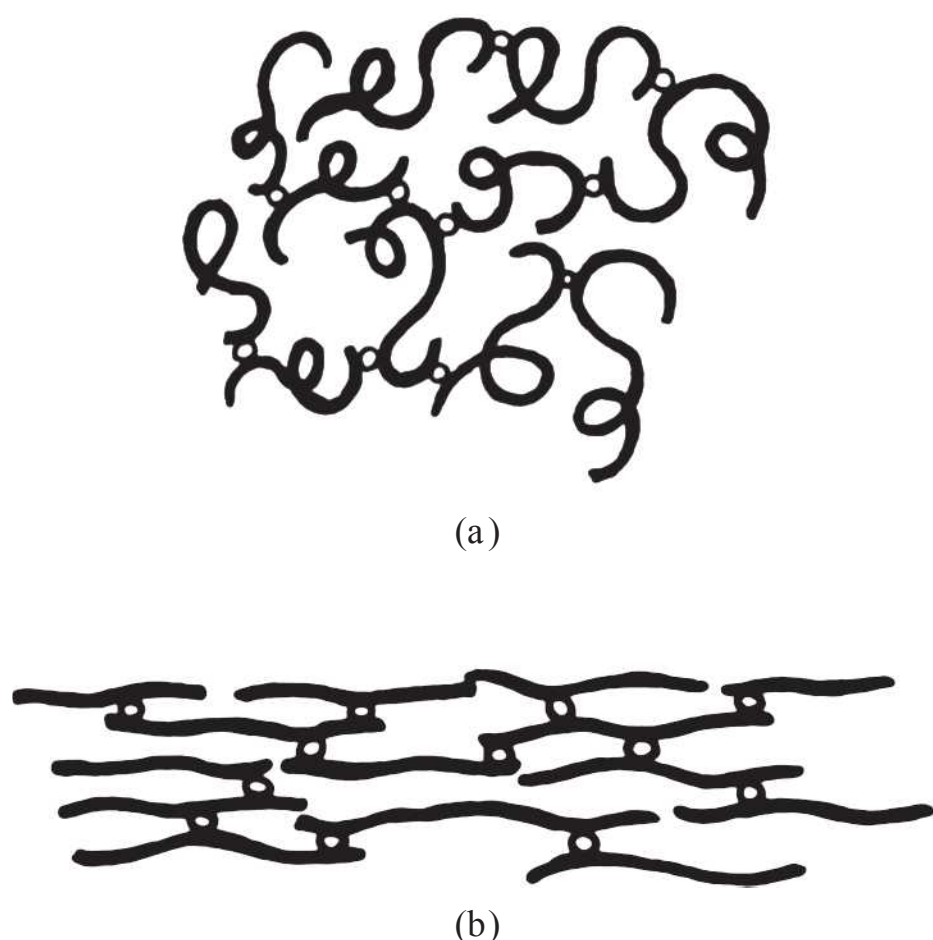
- Procollagen is converted into tropocollagen by the enzyme procollagen peptidase.
- Polymerisation of tropocollagen forms collagen fibrils.
- Aggregation of fibrils forms collagen fibres and fasciculi of fibres (Fig. 5.4).



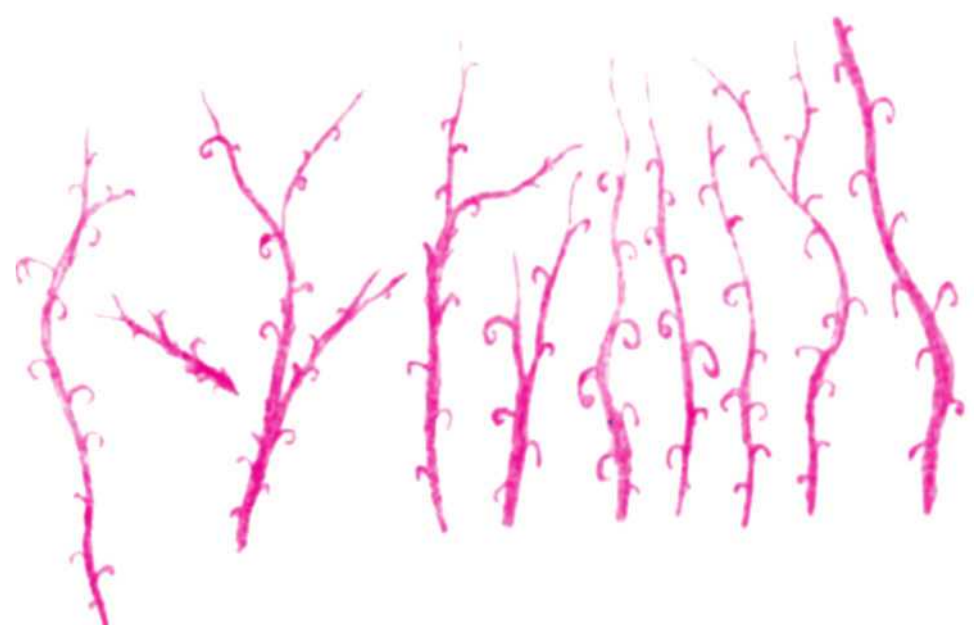
**Figure 5.4** Organisation of collagen fibres. Aggregation of collagen fibrils forms collagen fibres. Several collagen fibres are present in a fasciculus of collagen fibres.

**Elastic Fibres** (Figs 5.5 and 5.6)

- Elastic fibres have the property to stretch in response to tension and hence provide elasticity to the tissue.
- These fibres are thin and straight (after sectioning, they become wavy). They are thinner than collagen fibres. Individual fibres branch and form three-dimensional network.
- They consist of the protein elastin and microfibrils.
- Elastic fibres are eosinophilic. As mentioned earlier, collagen fibres are also eosinophilic; hence, in H&E stained preparations it is difficult to distinguish these two fibres. They can be distinguished in elastic Van Gieson stain preparations, wherein elastic fibres stain black and collagen fibres stain red.



**Figure 5.5** Elastic fibres in (a) relaxed state and (b) stretched state.

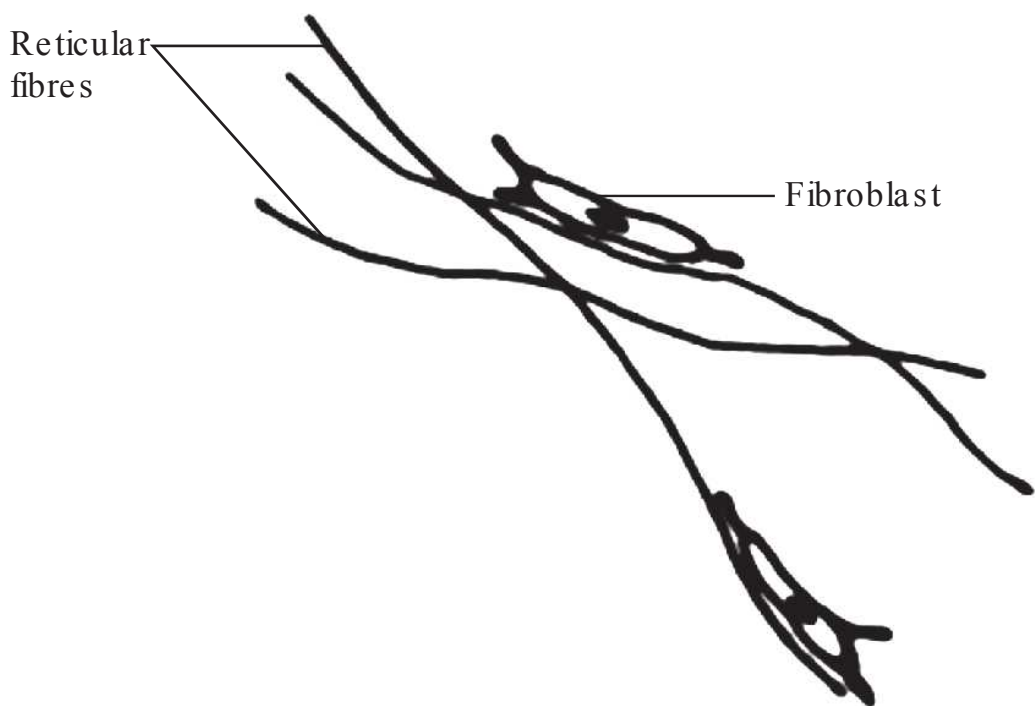


**Figure 5.6** Section of elastic fibres (H&E pencil drawing).

- Elastic fibres help restore normal shape of the tissue after distortion. These fibres are extremely elastic and can stretch and recoil; this is because a network of elastin molecules is formed by covalent bonding which can stretch and recoil.
- The tissues that have high concentration of elastic fibres (such as elastic cartilage) appear yellow in colour on gross appearance.
- These fibres are present in large numbers in skin, lungs, large blood vessels and elastic ligaments such as ligamentum nuchae.

**Reticular Fibres** (Fig. 5.7)

- These are thin fibres which make an extensive network.
- Reticular fibres consist of type III collagen; they are thinner than collagen fibres.
- They are not stained by H&E stain; they are stained black by silver salts.
- These fibres form the framework in lymph nodes, spleen, bone marrow, liver, basement membrane, etc., to provide support to the cells in these tissues.



**Figure 5.7** Reticular fibres.

**CELLS OF THE CONNECTIVE TISSUE**

- Cells of the connective tissue are classified as fixed and wandering cells (Table 5.1). See also Figure 5.1 for the illustration of these cells.

**Table 5.1** Connective Tissue Cells and Their Main Functions

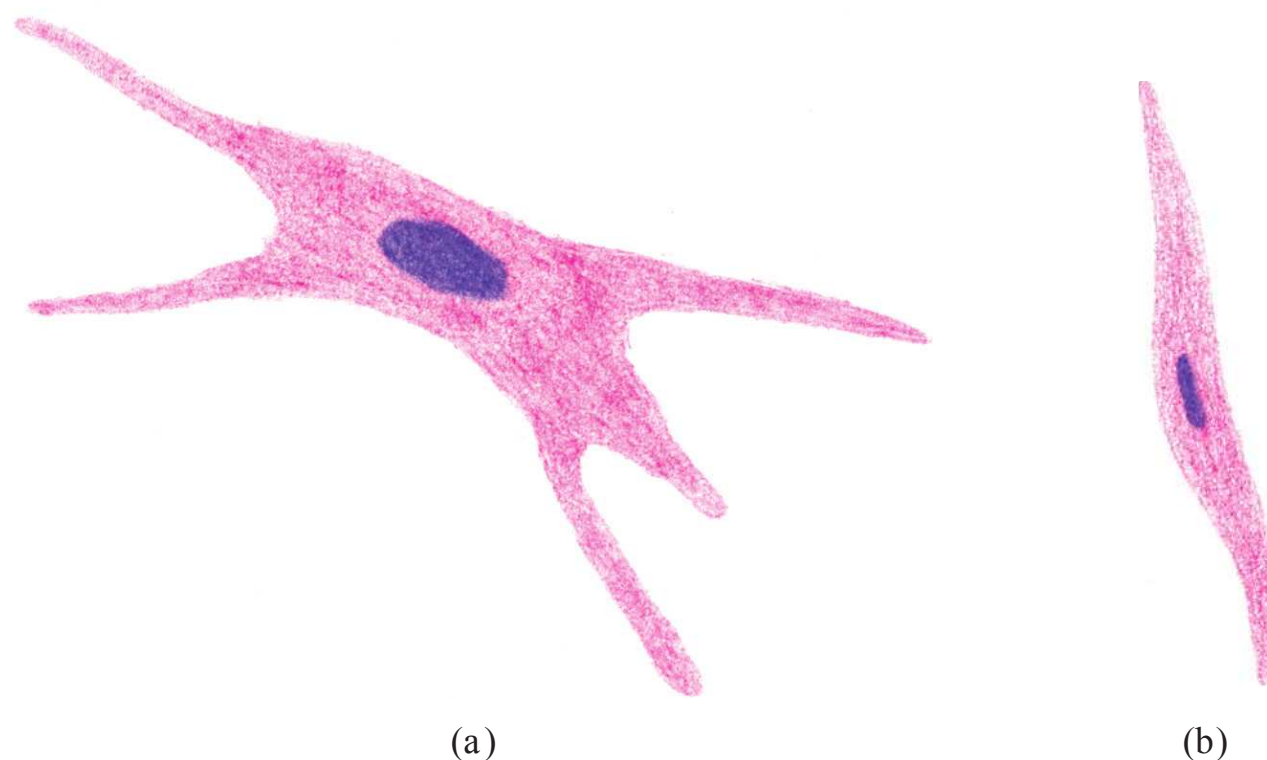
Cell type		Main functions
Fixed cells	Fibroblasts	Secrete and maintain the components of matrix
	Adipose cells	Store energy and act as thermal insulators
Wandering cells	Plasma cells	Provide defence and immunity
	Macrophages	
	Mast cells	
	Neutrophils	
	Eosinophils	
	Basophils	
	Lymphocytes	
	Monocytes	



- Fixed cells are those cells which originate and reside in the connective tissue. Fibroblasts and adipose cells are **fixed** cells.
- Wandering cells are those cells which originate in the bone marrow and migrate into the connective tissue. Plasma cells, macrophages, mast cells and leucocytes are wandering cells.
- All connective tissue cell types are derived **from** cells **of** embryonic mesenchyme (mesenchymal cells).

### **FIBROBLASTS**

- These are the most abundant cells in connective tissue.
- Active **fibroblast** has an abundant and branched cytoplasm, with a large and ovoid nucleus in the centre (Fig. 5.8).
- Quiescent **fibroblast** is smaller in size than active **fibroblast** and is spindle in shape with a flat nucleus. It is called **fbrocyte** (Fig. 5.8).
- Fibroblasts secrete collagen and elastin proteins and other components **of** matrix.



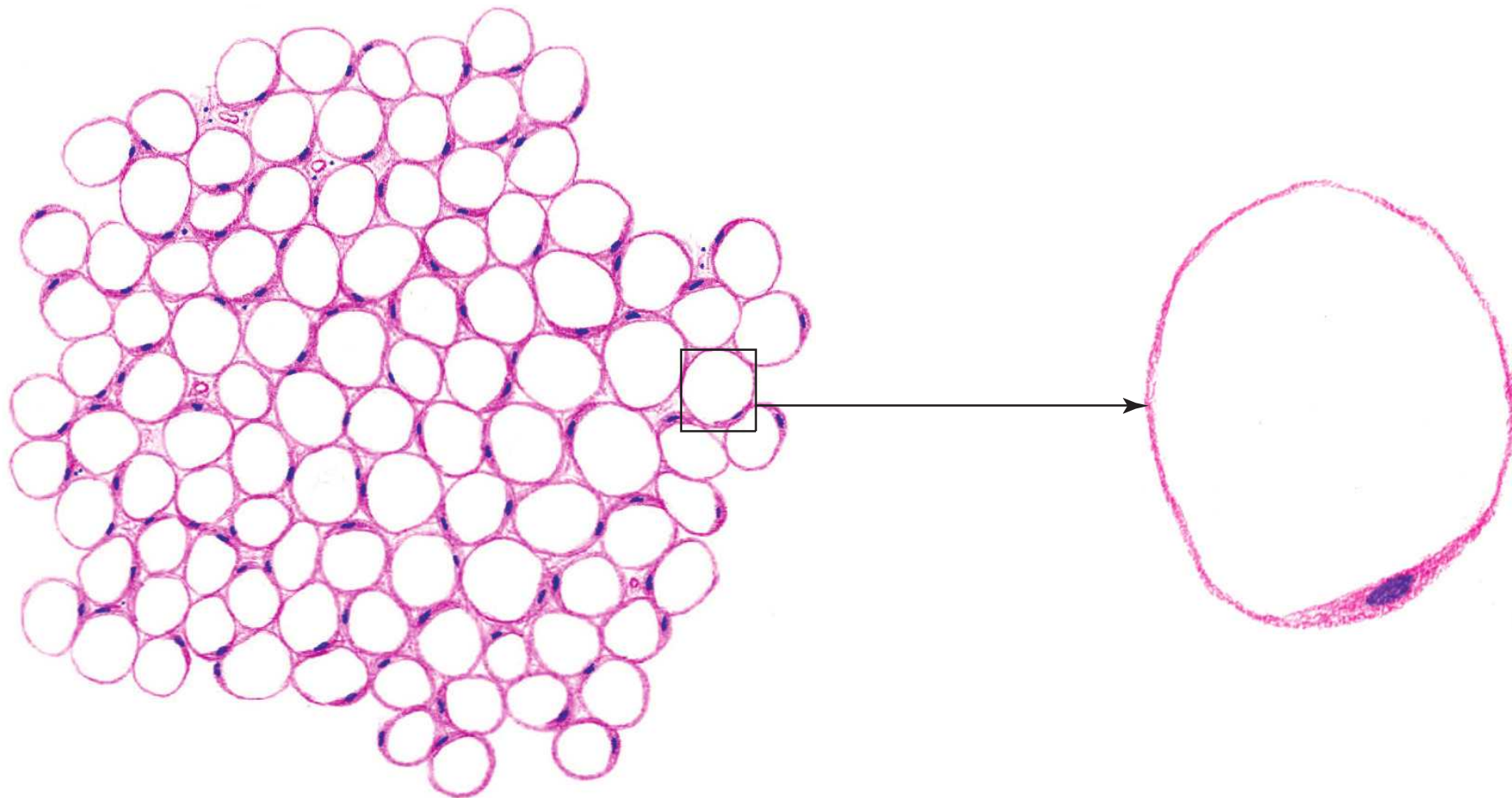
**Figure 5.8** (a) Fibroblast and (b) fbrocyte (H&E pencil drawing).

### **ADIPOSE CELLS (ADIPOCYTE)**

- Adipose tissue is a connective tissue specialised to store **fat** which is used as **fuel**; it also acts as a cushion and as a thermal insulator.
- It is made up **of** **fat** cells. Fat cells are also called adipocytes and can be present in isolation or in groups.
- There are two types **of** adipose tissues—unilocular (or yellow) and multilocular (or brown) adipose tissues.

#### **Unilocular Adipose Tissue**

- Almost all the adipose tissue in adults is **of** this type. It is present almost throughout the body underneath the skin as subcutaneous **fat** and acts as a thermal insulator.
- Its distribution is regulated by sex hormones.
- Adipose cells are round in shape; each cell has a single **fat** droplet.



**Figure 5.9** Unilocular adipose tissue in low magnification. Inset shows an adipocyte in high magnification. (H&E pencil drawing)

- During histological preparation, the fat droplet is lost; as a result only a thin rim of cytoplasm is left (Fig. 5.9).
- Nucleus is flattened and eccentric in position; hence, the cell appears as a signet ring.

### Multilocular Adipose Tissue

- It is present in embryos and newborns; it is greatly reduced in adults.
- It is called multilocular adipose tissue because in this type of adipose tissue each cell has multiple fat vacuoles.
- Adipose cells of multilocular adipose tissue are smaller in size than the cells of unilocular adipose tissue.
- These adipose cells have a single, centrally located, spherical nucleus.
- These contain large number of mitochondria.
- The multilocular adipose tissue is highly vascular. This gives the tissue its characteristic colour; hence, it is also called brown fat.

### PLASMA CELLS (Fig. 5.10)

- These cells are derived from B lymphocytes after antigenic stimulation, and they produce antibodies.
- These cells are large and ovoid in shape; their nuclei are spherical and eccentrically located. The nuclei have 'cartwheel' appearance due to the clumps of chromatin arranged in a radiating manner.

### MACROPHAGES

- These are derived from precursor cells present in the blood, the monocytes, which originate in the bone marrow and enter into the bloodstream.
- Apart from connective tissue, macrophages are present in other parts of the body as well. They are called histiocytes in connective tissue, Kupfer's cells in liver and microglia in central nervous system.
- They remove foreign bodies by phagocytosis. They belong to mononuclear phagocyte system.
- They take part in immune response by presenting the phagocytosed antigen to the lymphocytes.



## MAST CELLS

- These are ovoid cells with a spherical nucleus; they are characterised by abundant basophilic granules in their cytoplasm.
- They take part in the inflammatory response and hypersensitivity reactions.

## LEUCOCYTES (Fig. 5.10)

- These cells originate from bone marrow and migrate via the blood and lymph capillaries to the connective tissue.
- Leucocytes are classified into two groups: granulocytes and agranulocytes.
- Granulocytes are characterised by single segmented nuclei and cytoplasmic granules with specific contents. Neutrophils, eosinophils and basophils are the three different types of granulocytes.
- Agranulocytes are characterised by single unsegmented nuclei; these cells lack specific cytoplasmic granules. Lymphocytes and monocytes are the two different types of agranulocytes.

### Neutrophils

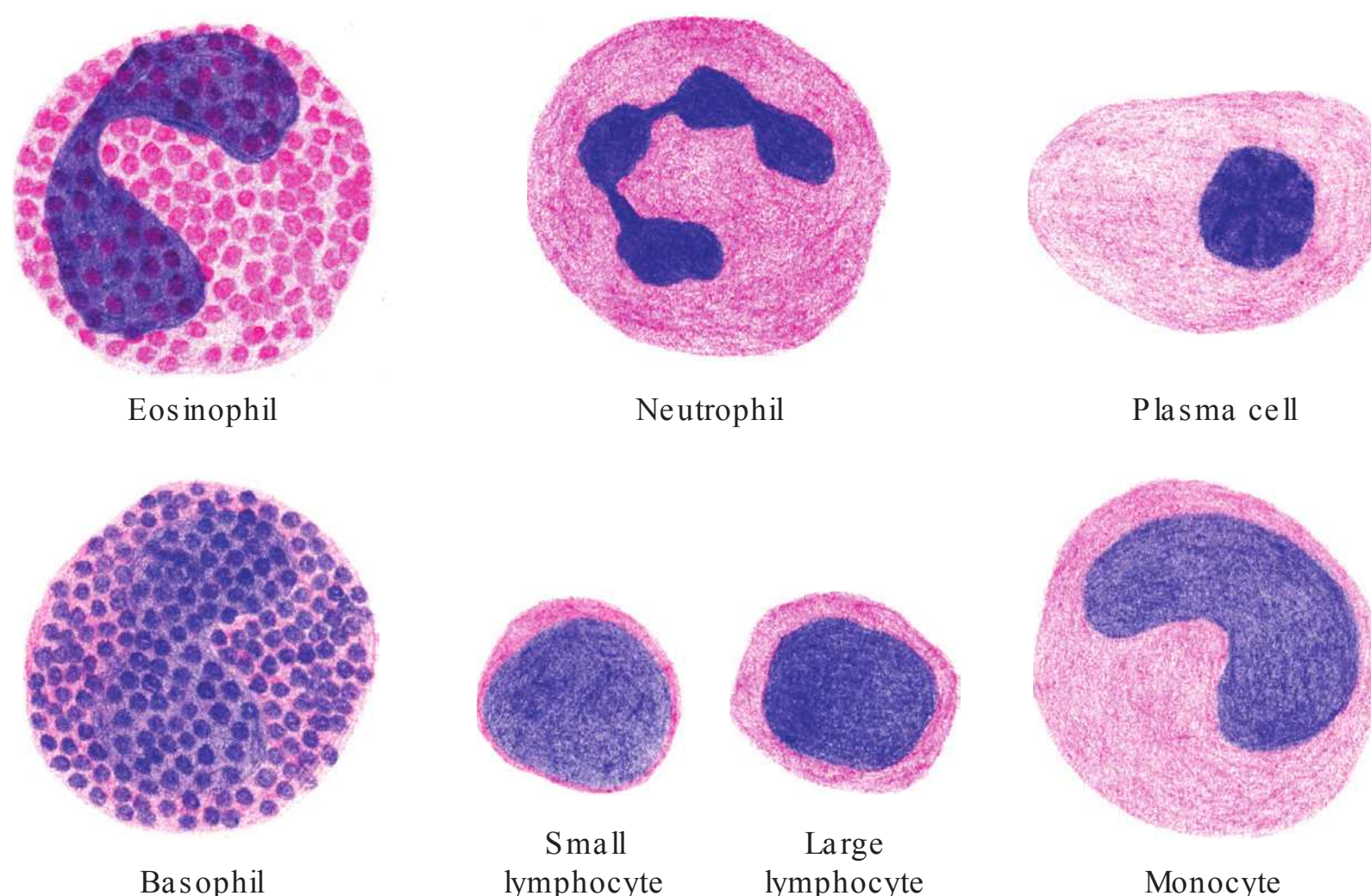
- These are the most abundant (50–70%) leucocytes present in blood.
- Their nuclei have 3–5 lobes (Fig. 5.10).
- They provide first line of defence against infective organisms.
- They phagocytose the microorganisms and destroy them by their enzymes.

### Eosinophils

- They constitute 1–5% of the leucocytes present in blood.
- They are characterised by the presence of bilobed nucleus (Fig. 5.10).
- These cells phagocytose antigen–antibody complexes.

### Basophils

- These are the least common leucocytes in blood (0–1%).
- In these cells, nucleus is segmented but not seen clearly due to the presence of dark, stained cytoplasmic granules (Fig. 5.10).
- These are phagocytic cells; their granules contain heparin and histamine.



**Figure 5.10** Wandering cells of connective tissue (H&E pencil drawing).



## Lymphocytes

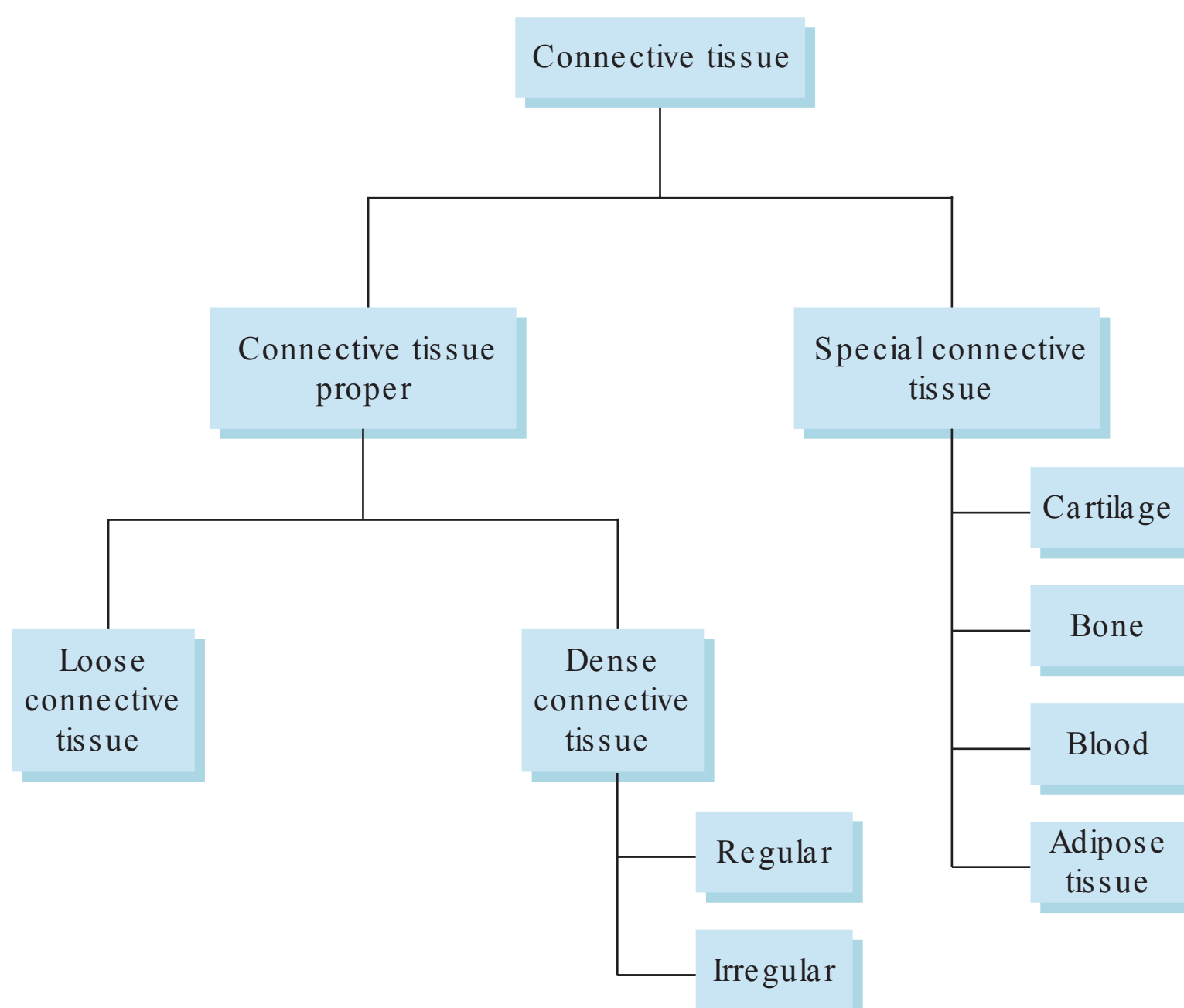
- These are the smallest leucocytes in size. They constitute 20–40% of the total leucocytes in blood.
- They are present throughout the body. They are most numerous in gastrointestinal, respiratory and genitourinary tracts.
- They have round nucleus, which is often eccentrically placed.
- In small lymphocytes, a thin rim of cytoplasm is present around the nucleus, whereas in large lymphocytes the rim of cytoplasm is wider than in small lymphocytes (Fig. 5.10).
- There are three types of lymphocytes—T lymphocytes, B lymphocytes and natural killer (NK) cells (for more details refer Chapter 11).
- They are responsible for immunological defence. T lymphocytes are responsible for cell-mediated immunity. B lymphocytes are responsible for humoral immunity. Natural killer (NK) cells bring about antibody-dependent cellular cytotoxicity.

## Monocytes

- These are the largest leucocytes in size. They constitute 1–10% of the total leucocytes in blood.
- They have eccentrically placed, horseshoe-shaped nucleus (Fig. 5.10).
- In the connective tissue, they differentiate into macrophages.

## TYPES OF CONNECTIVE TISSUE

- Connective tissue is classified based on the composition of its cellular and extracellular components and their arrangement.
- Connective tissue is broadly classified into two groups (Fig. 5.11):
  - (a) Connective tissue proper
  - (b) Special connective tissue

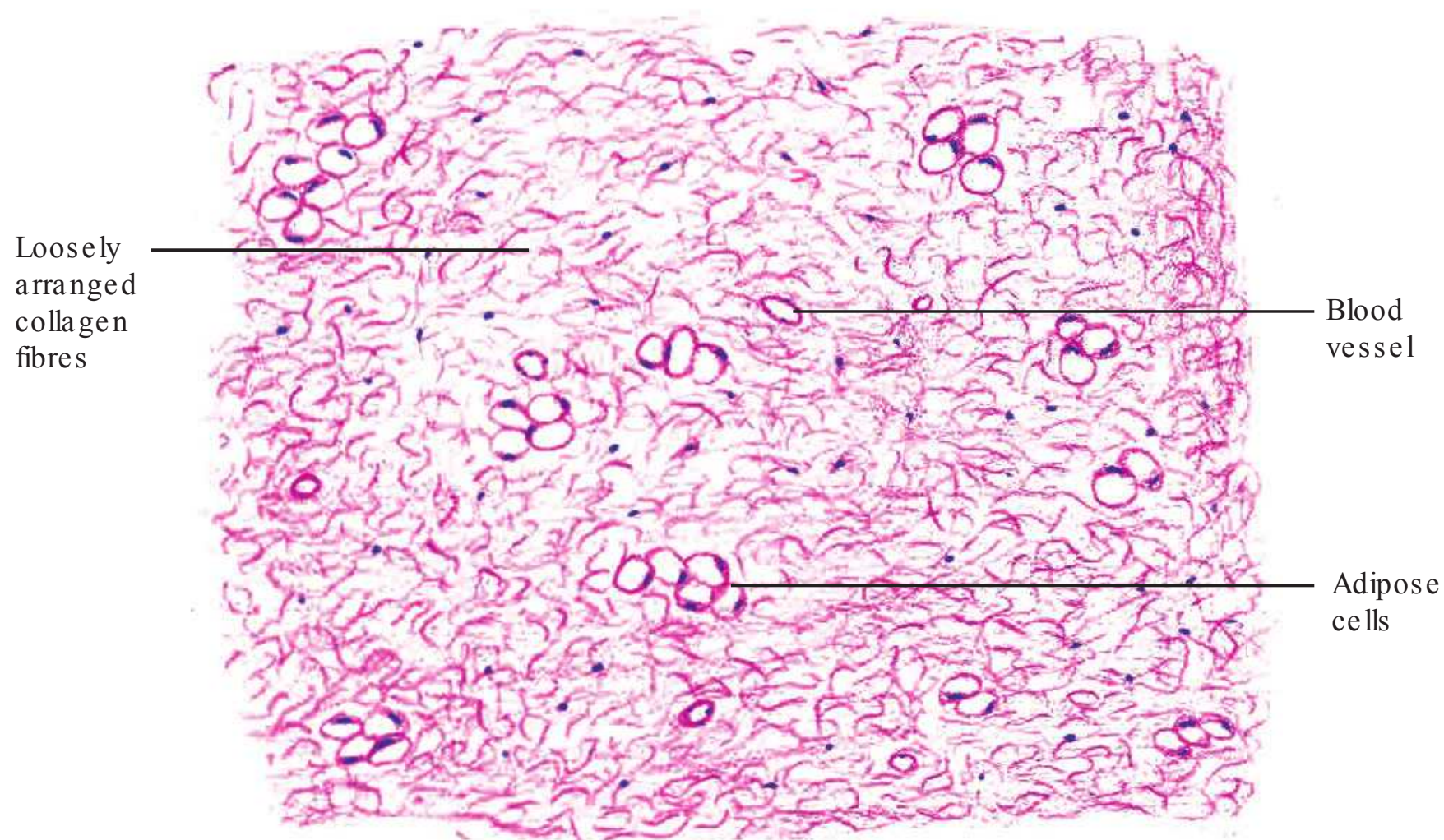


**Figure 5.11** Classification of connective tissue.

- Connective tissue proper includes those connective tissues in which fibrous component is predominant. Connective tissue proper includes loose (areolar) connective tissue and dense (regular and irregular) connective tissue.
- Special connective tissue is designed for specific functions and hence is present at specific locations. It includes adipose tissue, cartilage, bone and blood. (Cartilage and bone are dealt with in separate chapters).
- In general, the term connective tissue refers to connective tissue proper, while special connective tissues are referred to by their specific names (e.g. bone).

### LOOSE CONNECTIVE TISSUE (Fig. 5.12)

- It is also called loose areolar tissue.
- It consists of loosely arranged collagen fibres and abundant ground substance. Elongated nuclei of fibroblasts can be seen. Other cells of connective tissue are also present.
- It gets distorted easily; hence, it allows the tissue to move freely.
- It also supports the overlying epithelium. It is a vascular tissue; metabolites and oxygen diffuse through it to the epithelium (which is avascular).
- Example: Lamina propria and submucosa of various tracts (respiratory, gastrointestinal, urinary, etc.) and hypodermis.



**Figure 5.12** Loose connective tissue in low magnification (H&E pencil drawing).

### DENSE CONNECTIVE TISSUE

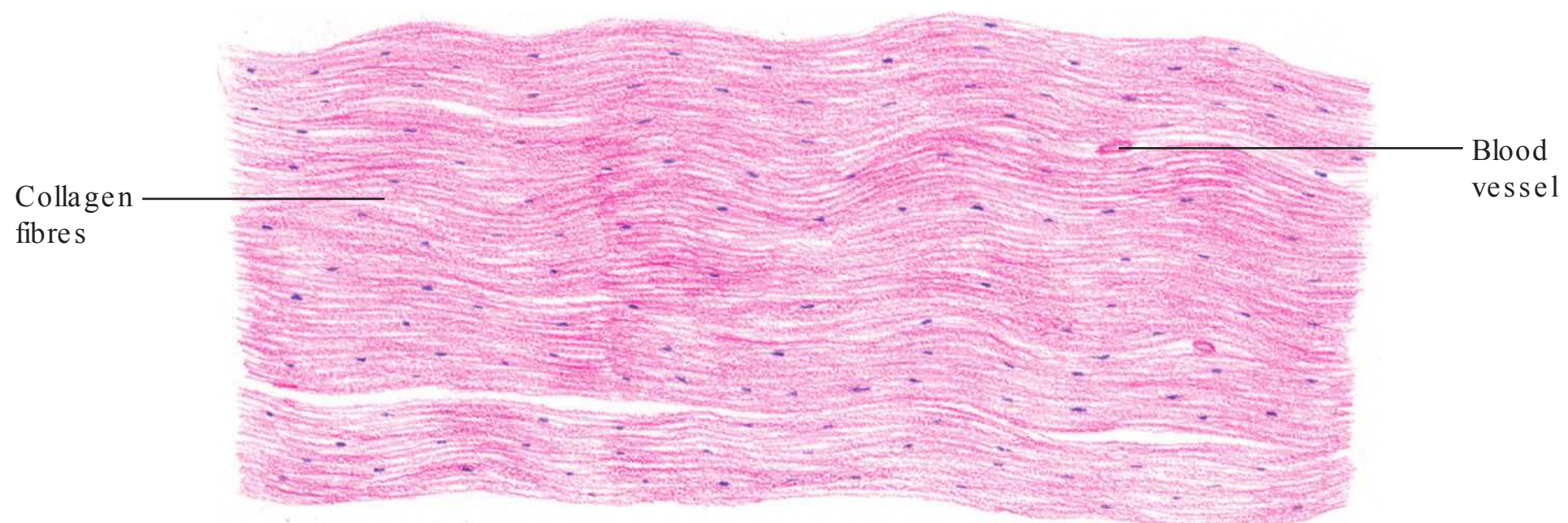
- It provides tensile strength to the tissue. It also offers protection to the underlying tissue.
- It has more fibres and less ground substance and cells.
- Based on the orientation of the fibres, it is of two types—dense regular and dense irregular connective tissues.

#### **Dense Regular Connective Tissue (Fig. 5.13)**

- Connective tissue is arranged in a definite pattern.



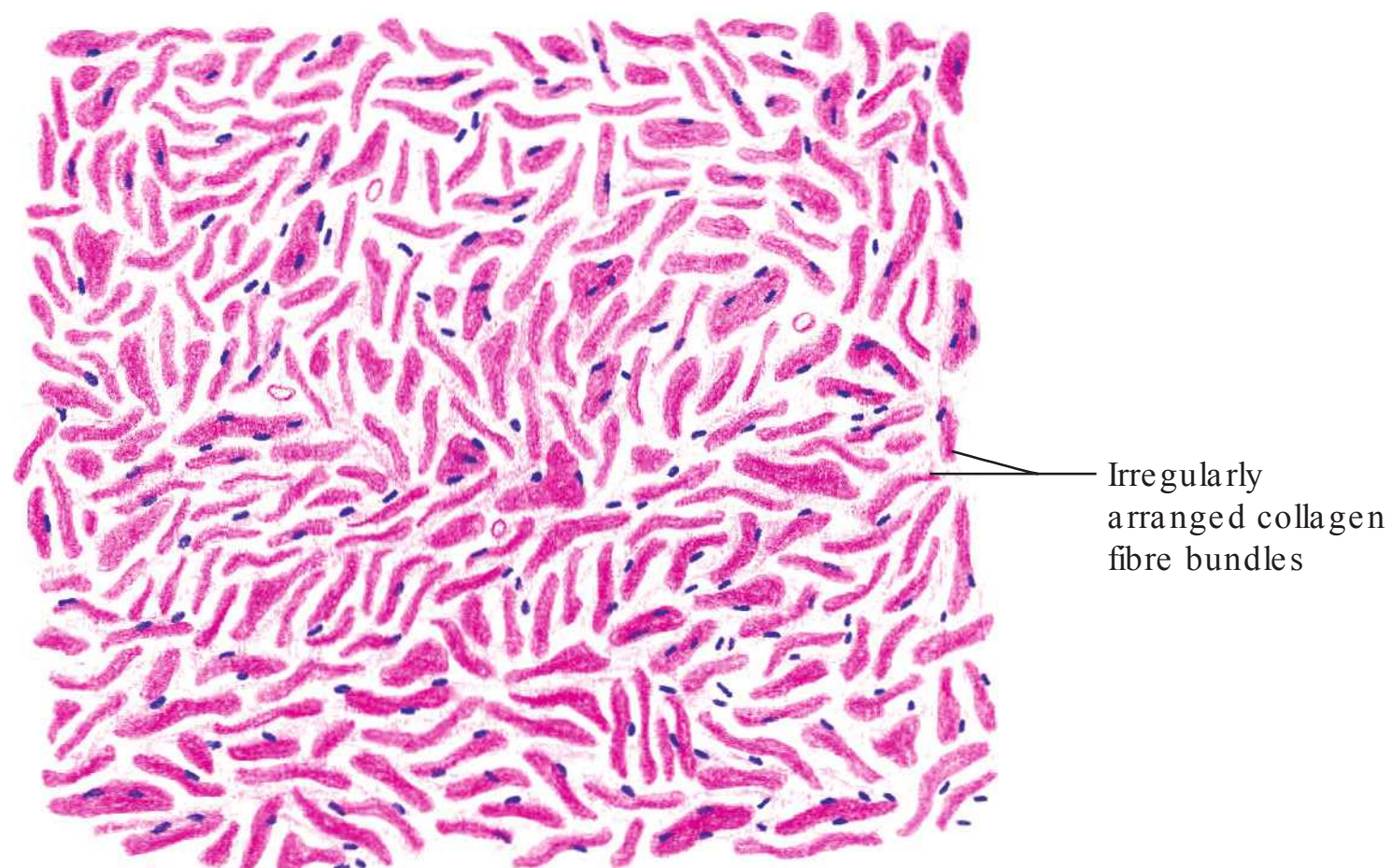
- Collagen fibres are aligned uniformly. This uniform alignment helps in transferring mechanical force. The force generated by a muscle is transferred to the bone through its tendon, which is a dense regular connective tissue.
- Example: Tendons and ligaments.



**Figure 5.13** Longitudinal section of tendon in low magnification showing dense regular connective tissue. Note the regular arrangement of collagen fibre bundles (H&E pencil drawing).

#### **Dense Irregular Connective Tissue** (Fig. 5.14)

- Collagen fibres are arranged irregularly.
- This tissue provides resistance to mechanical stress from all directions.
- Example: Reticular layer of the dermis.

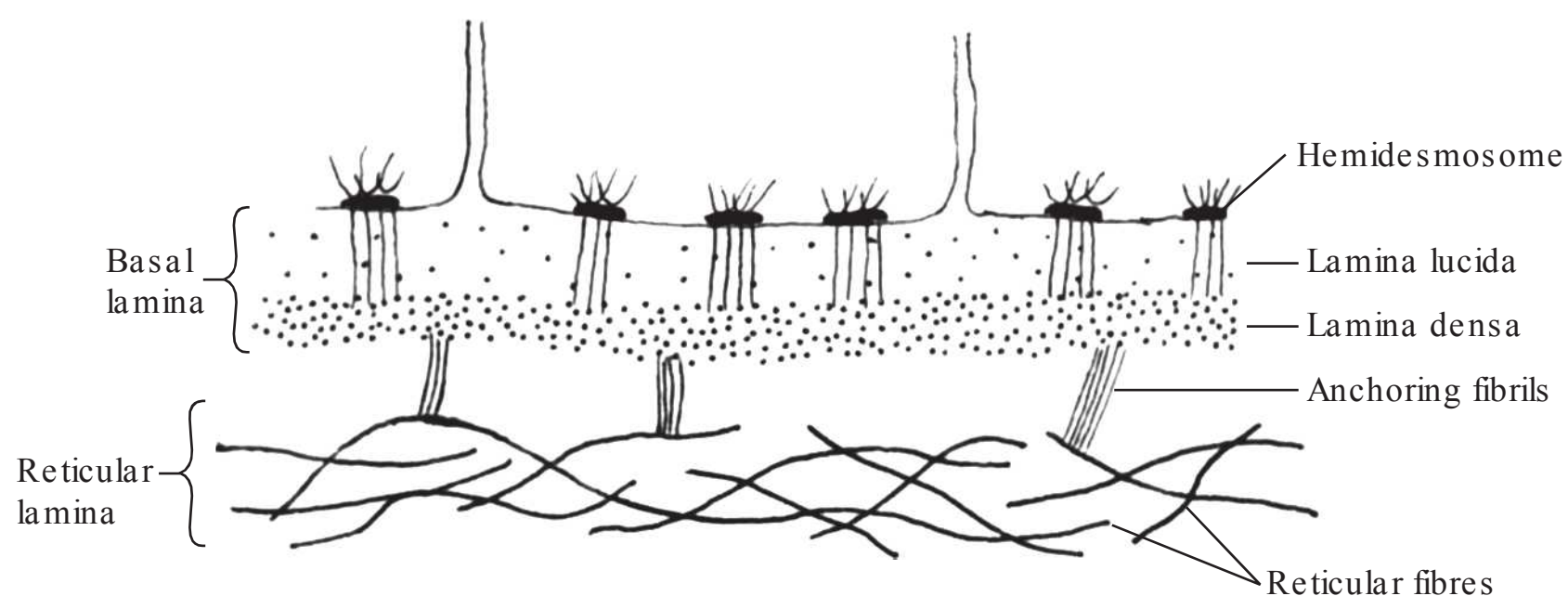


**Figure 5.14** Section of reticular layer of the dermis in low magnification showing dense irregular connective tissue (H&E pencil drawing).



## BASEMENT MEMBRANE

- It is a thin sheet of extracellular matrix secreted by epithelial cells which rest on it.
- Basement membrane consists of two layers: basal lamina and reticular lamina (Fig. 5.15). These components are visible only under an electron microscope.
- (a) Basal lamina is composed of type IV collagen, glycoproteins and proteoglycans. It consists of two layers: lamina lucida, which is a clear zone adjacent to the cell membrane, and lamina densa, which is a dense zone lying between lamina lucida and reticular lamina (Fig. 5.15).
- (b) Reticular lamina consists of reticular fibres, which are produced by cells of connective tissue.
- Anchoring fibrils, which consist of type VII collagen, extend from basal lamina to reticular lamina (Fig. 5.15).
- It should be noted that the terms basal lamina and basement membrane are often used interchangeably.
- Basal lamina associated with non-epithelial cells like muscle cells is referred to as external lamina.
- Functions: Basement membrane anchors the cells to the surrounding connective tissue. It acts as a filter; only certain substances can pass through the basement membrane.



**Figure 5.15** Basement membrane.

## CLINICAL CORRELATES

### Granulation Tissue

- After an injury, during wound healing, the fibroblasts multiply and synthesise extracellular matrix, new blood vessels are formed and all these together give rise to a new pink-coloured tissue called granulation tissue.

### Scars

- Scars are formed by fibroblastic activity during tissue repair. A scar is made up of collagen tissue, which is deposited by fibroblasts to replace damaged tissue. Excessive scar formation can give rise to hypertrophic scar; these are raised scars which do not grow beyond the original wound. When the excessive scar tissue grows beyond the original wound it is called keloid.

### Vitamin C Deficiency

- Vitamin C is required for synthesis of collagen; hence, deficiency of this vitamin results in bleeding and poor wound healing as seen in scurvy.

### Subcutaneous and Intramuscular Injection

- Drugs administered by these routes diffuse through the connective tissue.

KEYPOINTS

Components of Connective Tissue

- These are
  - (a) Cells,
  - (b) Fibres and
  - (c) Ground substance.
- Fibroblast synthesises all the components of the extracellular matrix.

Fibres

Fibre type	Organisation	Component	Location
<b>Collagen</b> (Fig. 5.13)	<ul style="list-style-type: none"><li>• Thick and wavy</li><li>• Individual fibre does not branch</li></ul>	Collagen protein	Dermis of the skin, tendon, fascia, basement membrane, etc.
<b>Elastic</b> (Fig. 5.6)	<ul style="list-style-type: none"><li>• Thin and straight</li><li>• Individual fibre branches</li></ul>	Elastin protein	Skin, lungs, blood vessels, etc.
<b>Reticular</b> (Fig. 5.7)	<ul style="list-style-type: none"><li>• Thin fibres</li><li>• They form a network</li></ul>	Collagen protein	Haematopoietic organs (lymph nodes, spleen and red bone marrow), to which they provide structural framework

Types of Connective Tissue

	Organisation	Examples
<b>Loose connective tissue</b> (Fig. 5.12)	Collagen fibres are loosely arranged	Lamina propria
<b>Dense regular connective tissue</b> (Fig. 5.13)	Collagen fibres are arranged regularly	Tendons, ligaments, etc.
<b>Dense irregular connective tissue</b> (Fig. 5.14)	Collagen fibres are arranged irregularly	Reticular layer of the dermis

SELF-ASSESSMENT

1. What are the functions of connective tissue?
2. What do you understand by ground substance?
3. List the different types of cells present in connective tissue and briefly discuss them.
4. Describe the adipose tissue.
5. Describe the different types of fibres present in connective tissue.
6. Describe the different types of connective tissue.

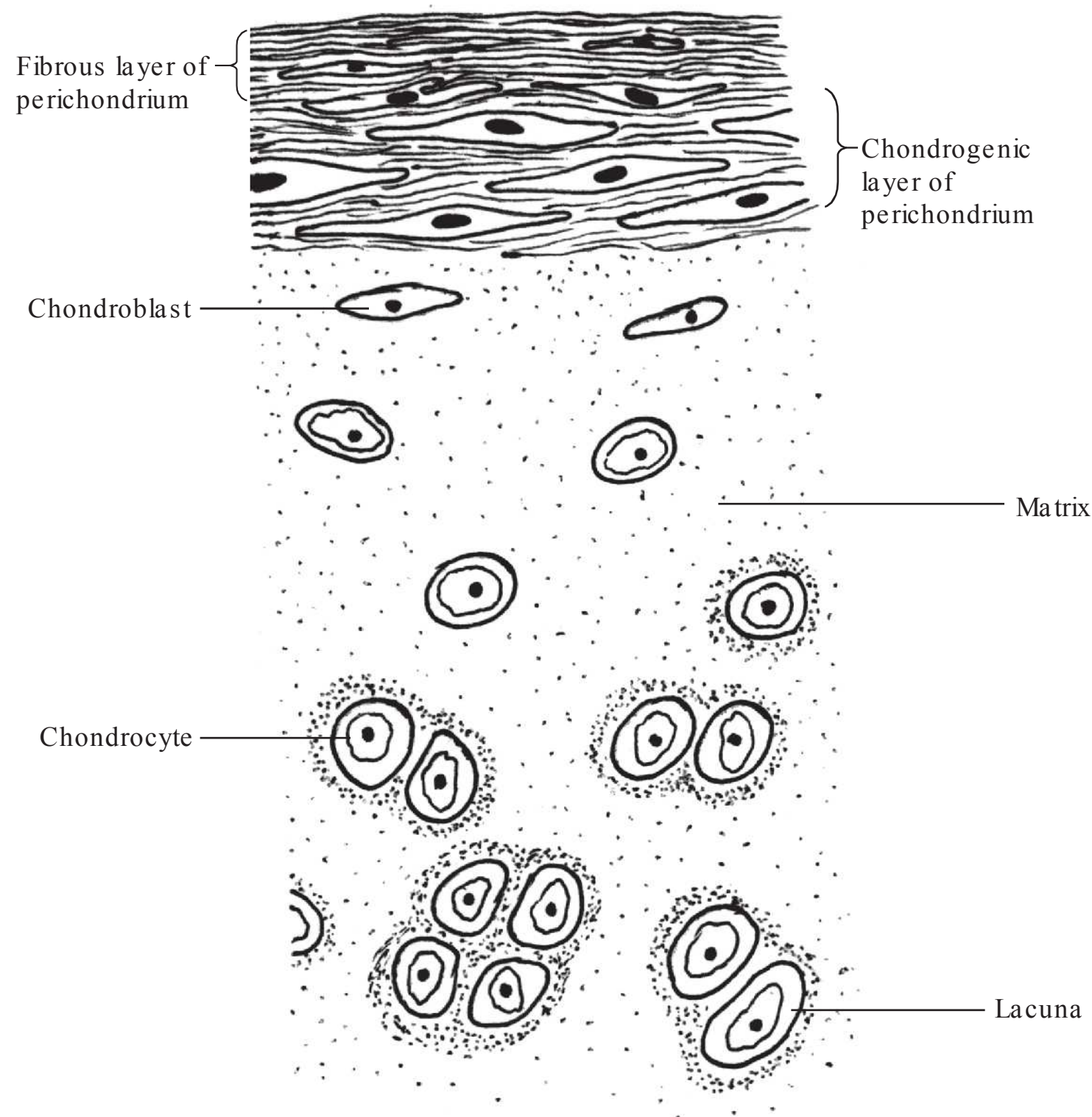


# Cartilage

- Cartilage is a special form of dense connective tissue characterised by elasticity and flexibility.
- Like other connective tissues, it also develops from mesenchymal cells and consists of cells and matrix (fibres and ground substance). However, it differs from other connective tissues in that it does not have blood supply, lymphatics or nerves.
- Cartilage, in most cases, is surrounded by perichondrium. The cells of cartilage are chondroblasts and chondrocytes. Ground substance is well hydrated and rich in proteoglycans.
- Functions: The major functions of cartilage are as follows:
  - (a) The articulating surfaces of the bones forming the joint are subjected to compressive forces during the movement of the joint. The articular cartilage that covers the articulating surface of the bone bears the compressive forces without undergoing permanent distortion. Hence, it acts as a cushion and protects the bone.
  - (b) In intrauterine life, the skeleton consists of cartilage; most of it is replaced by bones in later life. The epiphyseal plate of the long bones remains cartilaginous till the longitudinal growth of the bones is completed; it is this cartilaginous epiphyseal plate that is responsible for longitudinal-growth of the long bones.
- Nourishment: As mentioned earlier, the cartilage is avascular. It gets its nutrition and gases from the surrounding tissue, with the ground substance providing the medium for diffusion of nutrients and gases. The source of nourishment is the blood vessels present in the perichondrium (discussed later). The articular cartilage (which lacks perichondrium) derives its nourishment from synovial fluid that bathes the cartilage. Since the cartilage is an avascular tissue and it depends on the surrounding tissue for its nourishment, it has poor healing capacity. This also explains why cartilage cannot become very thick, since diffusion of nutrients and gases to the deeper tissue will be insufficient.

## PERICHONDRUM

- Perichondrium is a layer of dense connective tissue that surrounds most of the cartilages.
- It is derived from mesenchyme; the mesenchyme surrounding the developing cartilage becomes its perichondrium.
- Perichondrium consists of an outer fibrous layer and an inner chondrogenic layer (Fig. 6.1):
  - (a) Fibrous layer: The mesenchymal cells surrounding the cartilage differentiate into fibroblasts (Fig. 6.1). Fibroblasts form collagen fibres, and together they form the fibrous layer of perichondrium. (This layer is present on the outer aspect of the perichondrium.)
  - (b) Chondrogenic layer: This layer is present in the deeper aspect of perichondrium (the part of perichondrium which is in contact with the developing cartilage). Mesenchymal cells (chondrogenic cells of this layer) have the potential to differentiate into chondroblasts.



**Figure 6.1** Schematic diagram showing various components of cartilage (hyaline cartilage has been shown here).

- Perichondrium has blood supply, lymphatics and nerves, whereas cartilage does not have these. Hence, oxygen and metabolites diffuse from the perichondrium into the cartilage, as already mentioned before.

## COMPONENTS OF CARTILAGE

Cartilage consists of cells and extracellular matrix. The cells of cartilage are chondroblasts and chondrocytes. The extracellular matrix consists of fibres (collagen and elastic) and ground substance.

### CHONDROBLASTS

- Chondroblasts are oval-shaped cells, and they are present in the peripheral parts of the cartilage (Fig. 6.1).
- They are oriented parallel to the surface of the cartilage (Fig. 6.1).
- They are the precursors of chondrocytes.

### CHONDROCYTES

- The shape of these cells varies in different regions of the cartilage. In the peripheral part of the cartilage they are oval in shape, whereas in the deeper zone they are somewhat round in shape.
- Chondrocytes are present in small cavities in matrix called lacunae (singular: lacuna) (Fig. 6.1). In histological slides, there is a thin gap between the chondrocyte and the lacuna in which it resides. This is because of the shrinkage of the chondrocyte during slide preparation.
- Chondrocytes synthesise and secrete extracellular matrix.



## GROUND SUBSTANCE

- The ground substance is well hydrated, and the large component of water provides resiliency to the cartilage. Because of the resilient nature of the cartilage, it can get distorted without any damage and hence it provides flexible support to the surrounding tissues.
- The ground substance also provides the medium through which diffusion of gases and nutrients takes place.
- It is rich in proteoglycans. These are large molecules consisting of a core protein to which numerous glycosaminoglycans are attached.
- Glycosaminoglycans present in the cartilage are mainly chondroitin sulphate, hyaluronic acid and keratan sulphate.
- In hyaline cartilage, the matrix surrounding the lacuna (the territorial matrix of hyaline cartilage, described under 'Hyaline Cartilage') is more basophilic. This is because of the high concentration of proteoglycans in the matrix around the lacuna.

## TYPES OF CARTILAGE

- There are three types of cartilage depending on the varying proportion of the matrix. These are
  - (a) Hyaline cartilage,
  - (b) Elastic cartilage and
  - (c) Fibrocartilage.

## HYALINE CARTILAGE

- Hyaline cartilage is the most abundant type of cartilage in the body.
- It appears whitish blue and semi-transparent on gross appearance.
- Examples: Nasal septum, tracheal rings, articular surfaces of the moveable joints, costal cartilages, epiphyseal plate and foetal skeleton.

## MICROSCOPIC FEATURES (Fig. 6.2; PMG 6.1)

It consists of cells and matrix, as mentioned earlier. At most of the locations, hyaline cartilage is covered by perichondrium.

### Perichondrium

- The layers of perichondrium (fibrous and chondrogenic) are the same as described previously.
- Except the articular cartilage of joints, all hyaline cartilages have perichondrium. The articular cartilage gets its nutrition and oxygen from the synovial fluid.

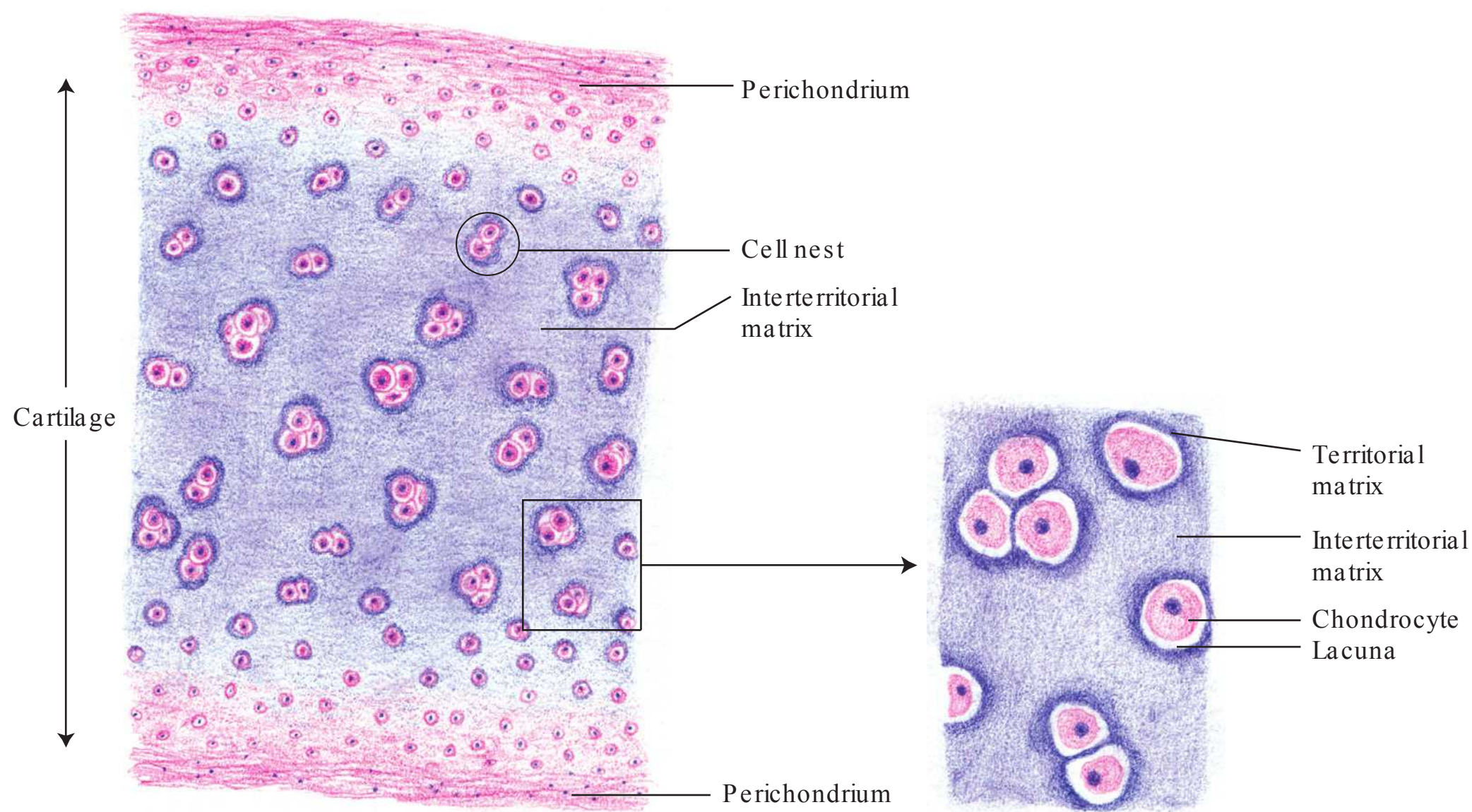
### Cells

- In the inner part of the cartilage, chondrocytes are arranged in clusters. These clusters are called cell nests (isogenous groups). Each cell nest usually contains two to eight mature chondrocytes.
- In the peripheral part of the cartilage, chondrocytes are less differentiated. They are ovoid in shape and they are single.

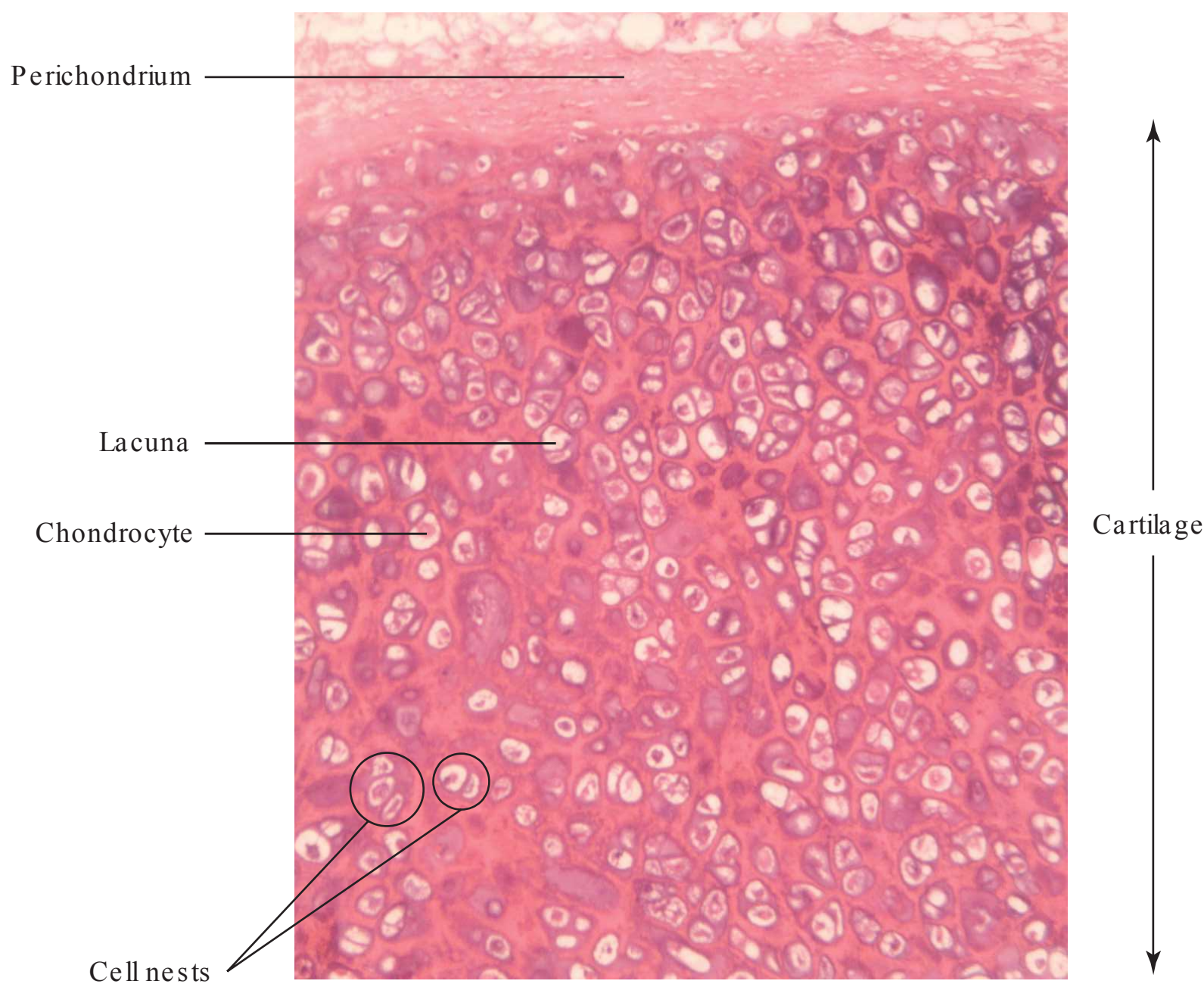
### Matrix

- The matrix is basophilic; around the lacuna it is more intensely basophilic and is called territorial matrix. In between the territorial matrix is interterritorial matrix (less basophilic than territorial matrix).





**Figure 6.2** Section of hyaline cartilage in low magnification. Inset shows a portion of cartilage in high magnification. (H&E pencil drawing)



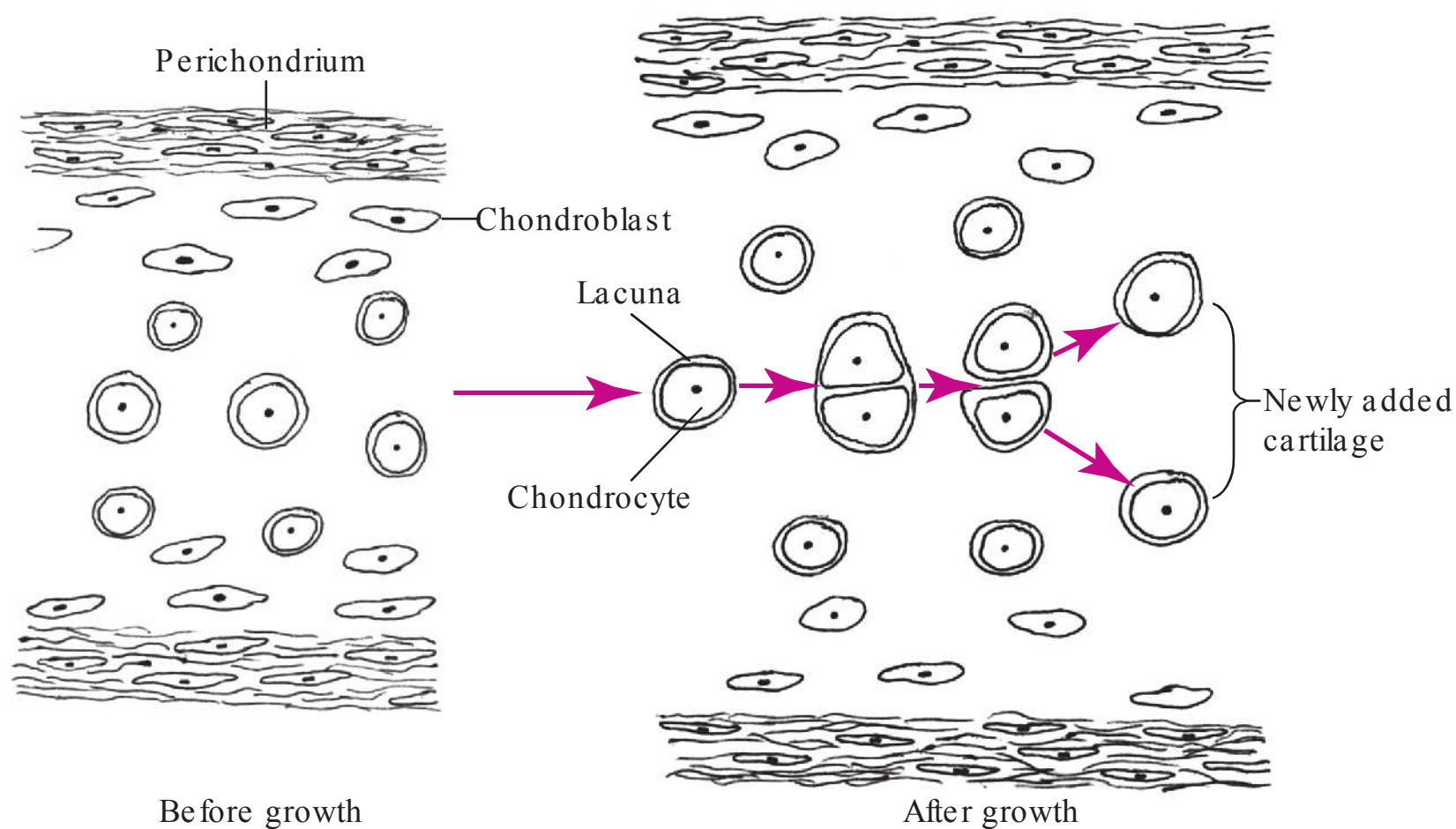
**PMG 6.1** Hyaline cartilage (H&E stain, X10).



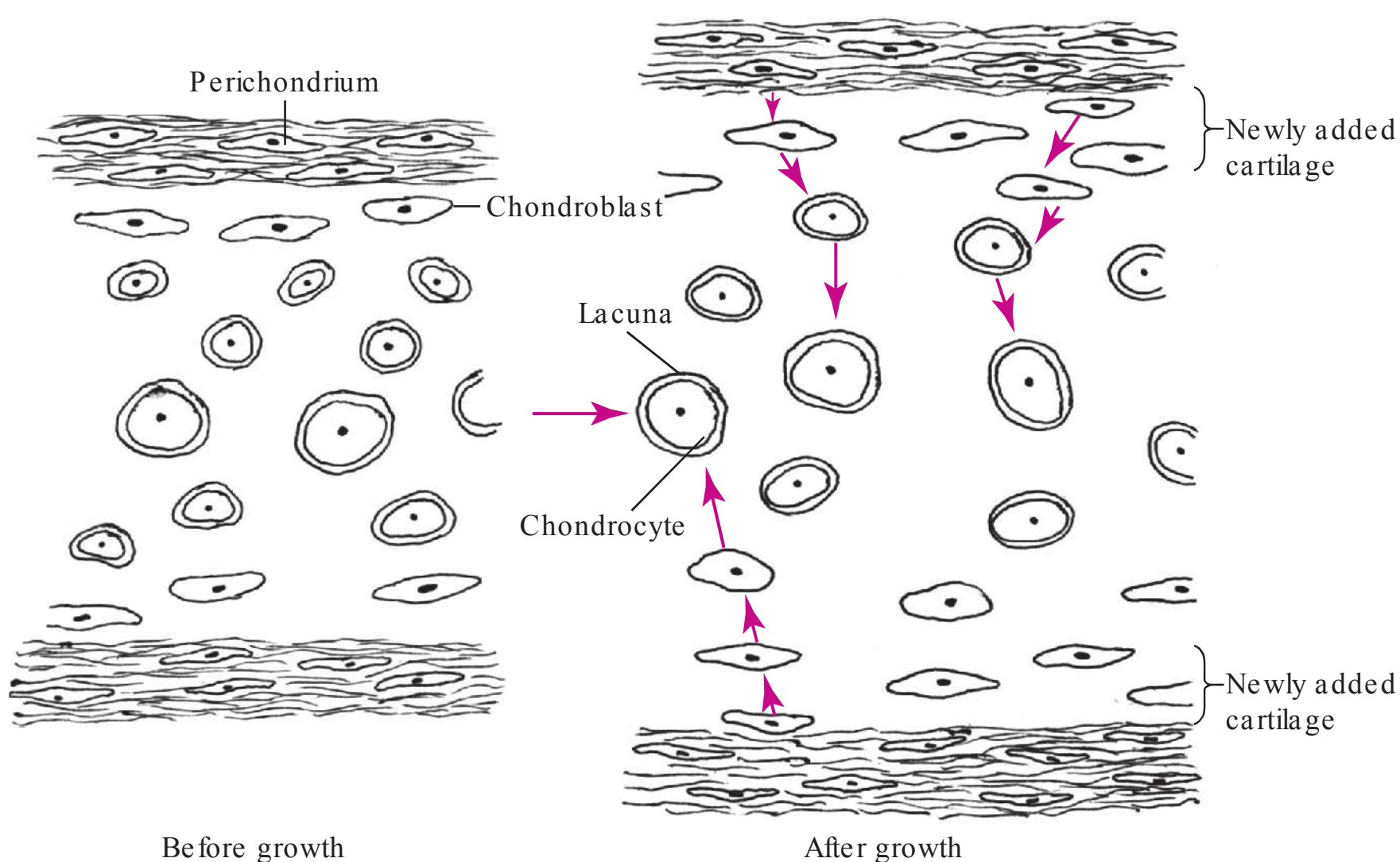
- It has type II collagen. In H&E stained histological slides, the collagen fibres cannot be distinguished from the matrix. This is because the refractive indices of collagen and the ground substance are the same; as a result, the fibres cannot be distinguished from the matrix.

### DEVELOPMENT AND GROWTH OF THE HYALINE CARTILAGE

- In the site where cartilage is to form, mesenchymal cells proliferate to form clusters. Their processes disappear and they are transformed into chondroblasts.
- Chondroblasts secrete matrix, and as more and more matrix is secreted, the chondroblasts move apart.
- They increase in size and are transformed into chondrocytes, which are surrounded by matrix.
- Mesenchyme surrounding the developing cartilage becomes perichondrium.
- Cartilage grows by two different methods: interstitial growth and appositional growth (Figs 6.3 and 6.4).



**Figure 6.3** Interstitial growth. Note the expansion of cartilage from inside.



**Figure 6.4** Appositional growth. Note that the newly formed cartilage is added to the superficial parts of pre-existing cartilage.

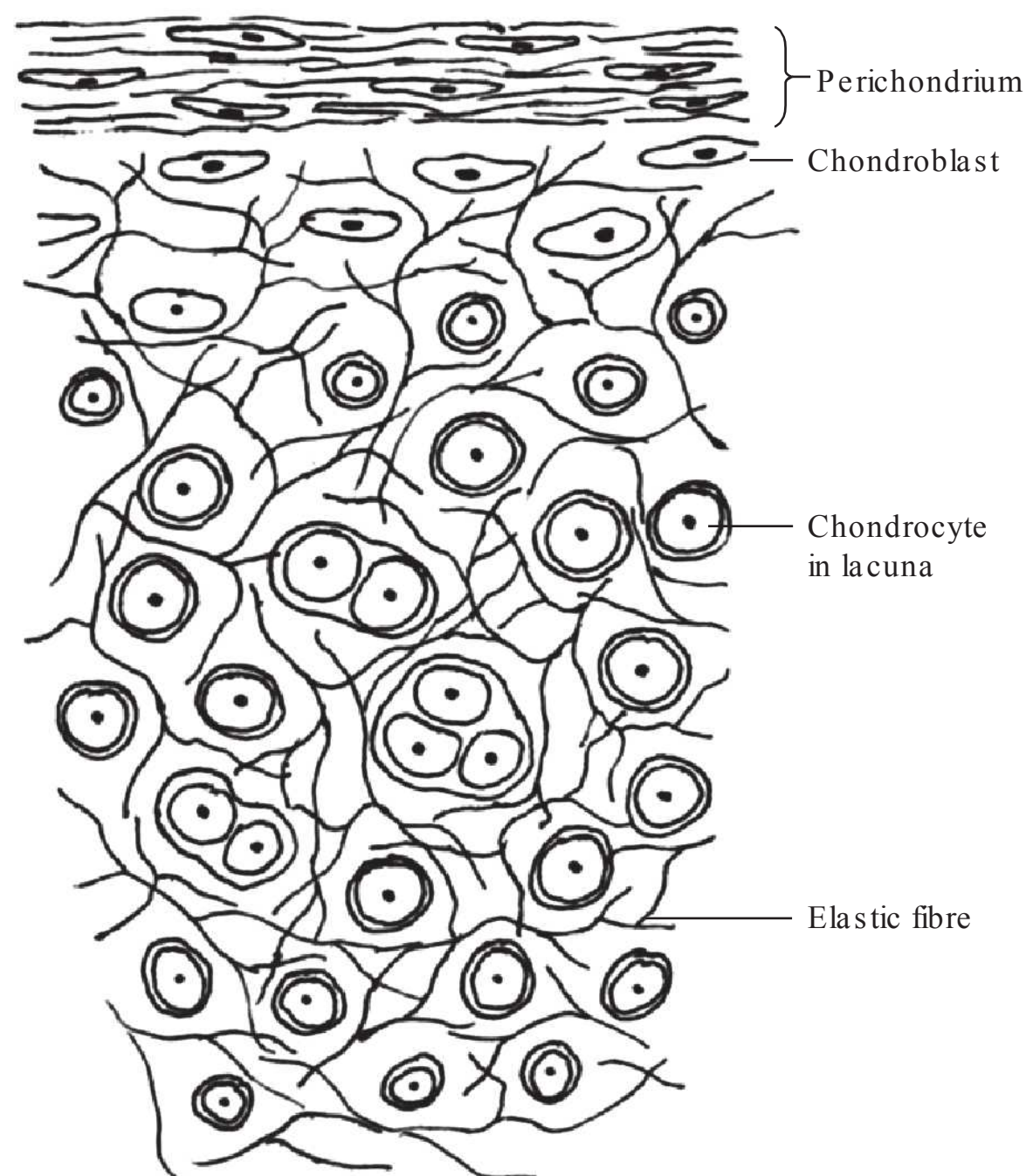
- (a) Interstitial growth: In this type of growth, the pre-existing chondrocytes divide and the newly formed cells secrete matrix. As a result, cells are pushed apart, causing the cartilage to expand from inside (Fig. 6.3).
- (b) Appositional growth: In this type of growth, cells in the chondrogenic layer of perichondrium differentiate to form chondroblasts. The newly formed cells and matrix are added in the superficial parts of the pre-existing cartilage (Fig. 6.4).

## ELASTIC CARTILAGE

- Elastic cartilage is present in places where more flexible support is needed.
- Examples: Auricle of the ear, walls of the external auditory canal, eustachian tube and epiglottis.
- Growth of elastic cartilage is similar to that of hyaline cartilage.
- It appears yellow on gross appearance due to the presence of elastic fibres. In H&E stain, elastic fibres are eosinophilic; however, they are better seen in sections stained with elastic Van Gieson stain, in which they appear black.

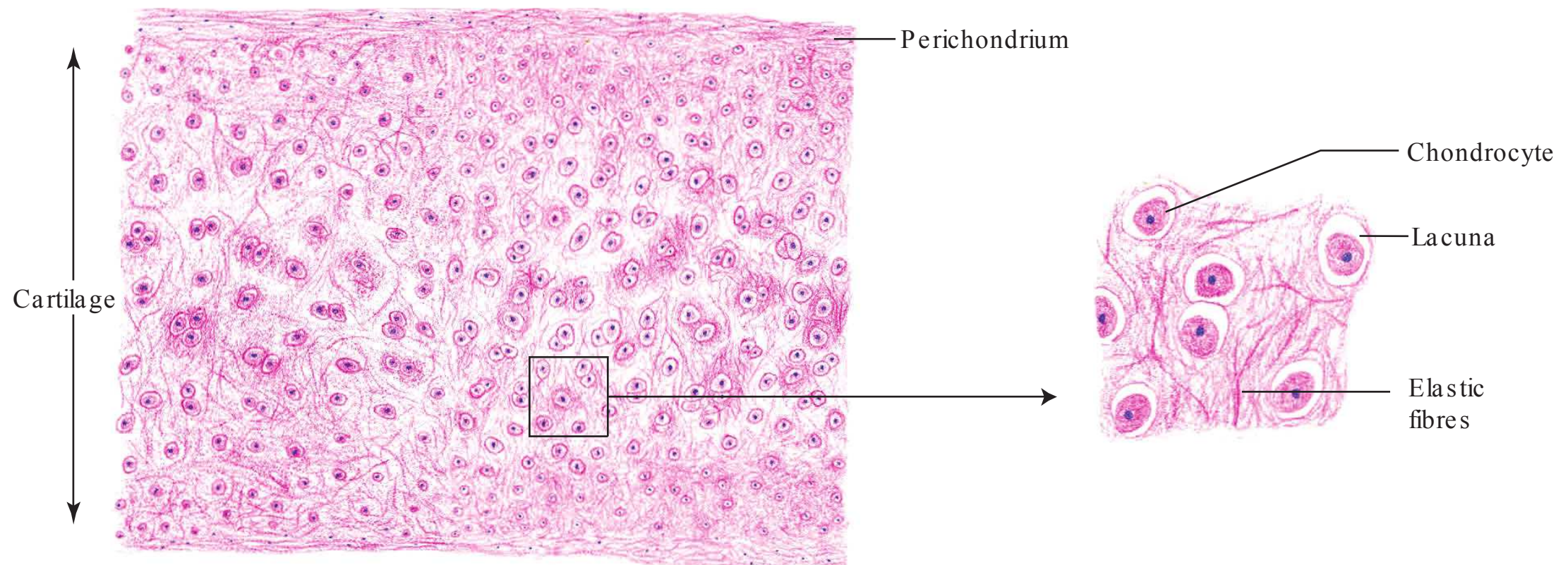
### MICROSCOPIC FEATURES (Figs 6.5 and 6.6; PMG 6.2)

- Elastic cartilage is structurally similar to hyaline cartilage, with a few differences:
  - (a) It has elastic fibres in addition to collagen fibres in the matrix.
  - (b) Cell nesting is not as much as in hyaline cartilage.
  - (c) Chondrocytes are closely packed, as the number of chondrocytes is more and amount of matrix is less, compared to hyaline cartilage (Figs 6.5 and 6.6; PMG 6.2).
- Perichondrium is present.

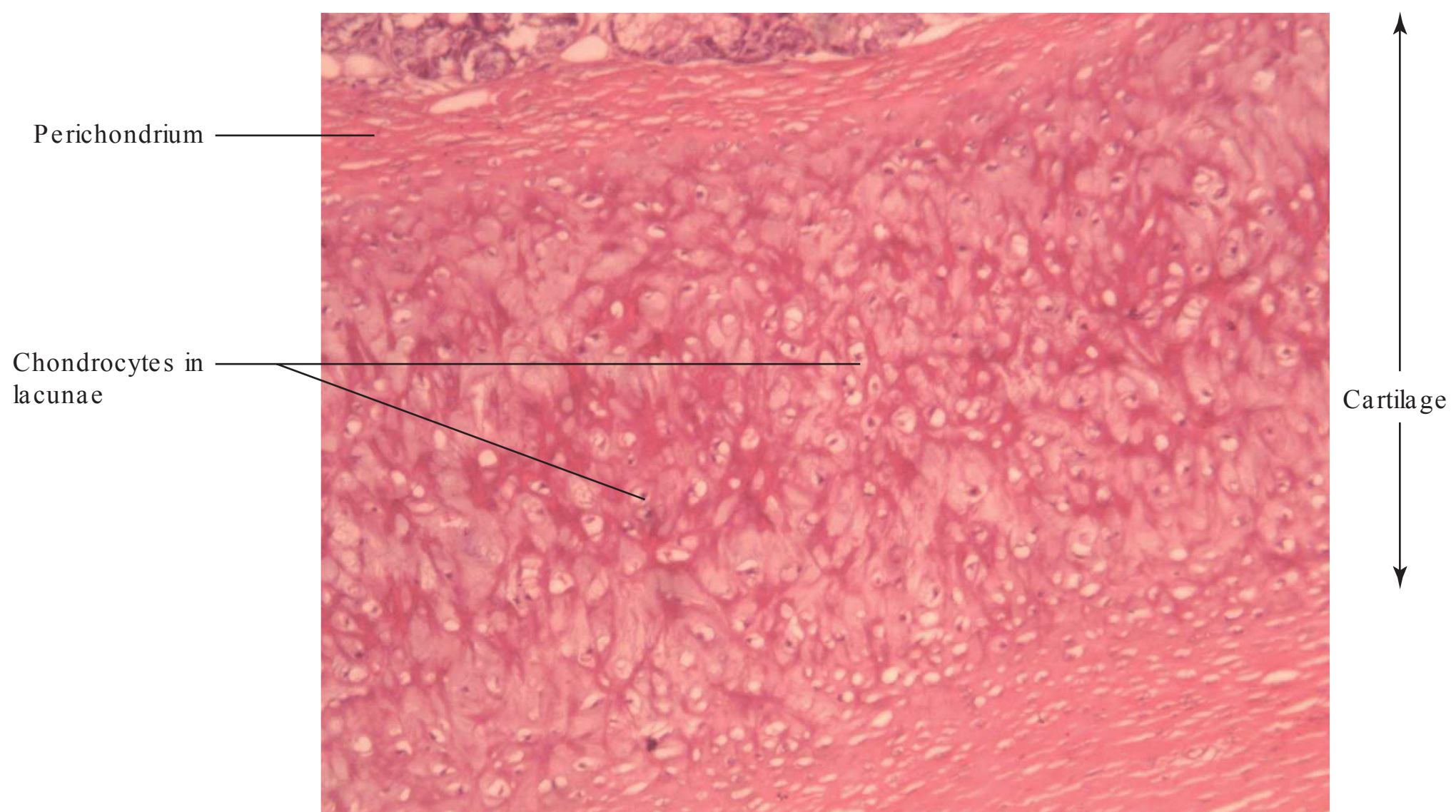


**Figure 6.5** Schematic diagram of elastic cartilage.





**Figure 6.6** Section of elastic cartilage in low magnification. Inset shows a portion of cartilage in high magnification. (H&E pencil drawing)



**PMG 6.2** Elastic cartilage (H&E stain, X10).

## FIBROCARILAGE

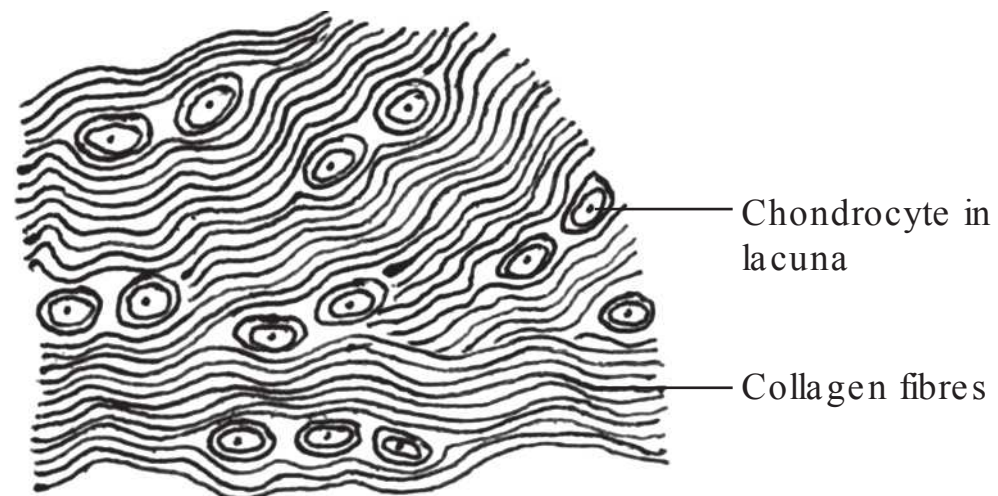
- Fibrocartilage provides tensile strength in the region where it is located.
- Examples: Intervertebral disc and the articular cartilage in pubic symphysis.

### MICROSCOPIC FEATURES (Figs 6.7 and 6.8; PMG 6.3)

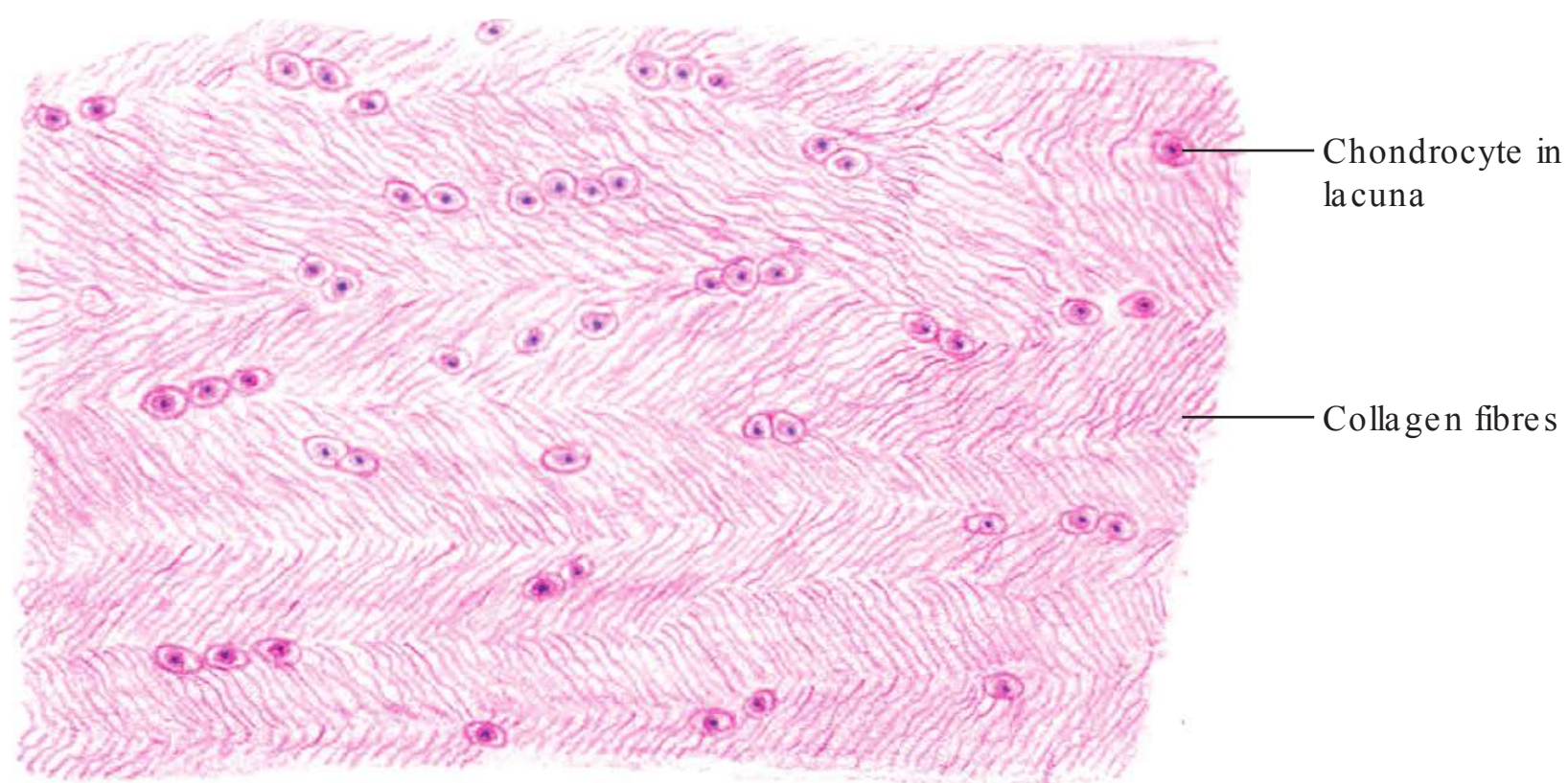
- It is devoid of perichondrium.



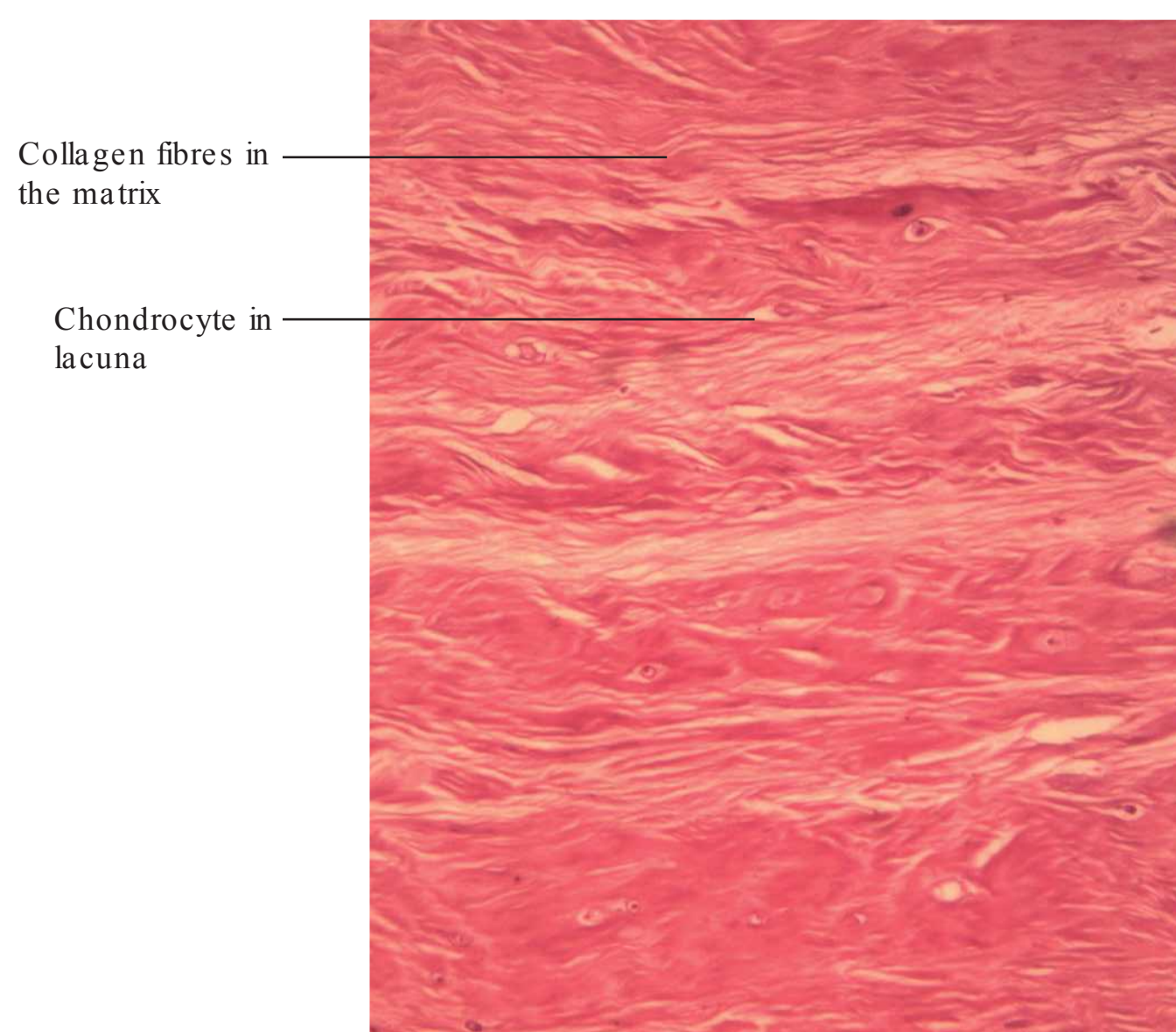
- It consists of rows of collagen fibres and ground substance. Collagen fibres (type I) are oriented in the direction of the stress.
- Chondrocytes are arranged in rows between the layers of collagen, within the lacunae in the matrix.



**Figure 6.7** Schematic diagram of fibrocartilage.



**Figure 6.8** Section of fibrocartilage in low magnification (H&E pencil drawing).



**PMG 6.3** Fibrocartilage (H&E stain, X10).



CLINICAL CORRELATE

Tumours

- Benign tumours are more common in cartilage. Chondroma refers to the benign tumour of cartilage, and chondrosarcoma is the malignant tumour.

KEYPOINTS

Types of Cartilage

	Hyaline cartilage (Fig. 6.2; PMG 6.1)	Elastic cartilage (Figs 6.5 and 6.6; PMG 6.2)	Fibrocartilage (Figs 6.7 and 6.8; PMG 6.3)
Perichondrium	<ul style="list-style-type: none"><li>• Present (except in articular cartilage)</li></ul>	<ul style="list-style-type: none"><li>• Present</li></ul>	<ul style="list-style-type: none"><li>• Absent</li></ul>
Cell (type and organisation) and matrix	<ul style="list-style-type: none"><li>• Cell nest is well defined. Two to eight chondrocytes are present in a cell nest</li><li>• Matrix surrounding the cell nest is more basophilic (territorial matrix), and it is surrounded by less basophilic (interterritorial) matrix</li></ul>	<ul style="list-style-type: none"><li>• It is structurally similar to hyaline cartilage with a few differences:<ul style="list-style-type: none"><li>(a) Elastic fibres are also present in the matrix</li><li>(b) Cell nesting is not well defined</li><li>(c) There is a higher number of chondrocytes and less matrix</li></ul></li></ul>	<ul style="list-style-type: none"><li>• Alternating layers of collagen fibres and ground substance are present</li><li>• Chondrocytes are arranged in rows between the layers of collagen, within lacunae</li></ul>
Fibre	<ul style="list-style-type: none"><li>• Type II collagen</li></ul>	<ul style="list-style-type: none"><li>• Elastic fibres and type II collagen</li></ul>	<ul style="list-style-type: none"><li>• Type I collagen</li></ul>
Examples	<ul style="list-style-type: none"><li>• Nasal septum, tracheal rings, articular surfaces of moveable joints and epiphyseal plate</li></ul>	<ul style="list-style-type: none"><li>• Auricle of ear, the walls of external auditory canal, eustachian tube and epiglottis</li></ul>	<ul style="list-style-type: none"><li>• Intervertebral disc</li></ul>

SELF-ASSESSMENT

1. What is perichondrium? Describe the two layers of perichondrium.
2. Describe the microscopic features of different types of cartilages. Give examples.
3. Describe the different types of growth that occur in hyaline cartilage.

# Bone

- Bone is a dense connective tissue specialised for support.
- Like other connective tissues, bone also consists of cells and extracellular matrix, but unlike other connective tissues, the extracellular matrix in bone is calcified, which makes it hard and rigid.
- Bone is a dynamic tissue; it constantly undergoes changes in response to physical stresses and hormonal changes.
- Functions
  - (a) The bone provides a rigid framework to the body and protects various organs.
  - (b) It is the storehouse of calcium and phosphorus.
  - (c) It contains bone marrow, which is a haematopoietic tissue.

## COMPONENTS OF THE BONE

The bone consists of cells and matrix. There are three types of cells in the bone: osteoblasts, osteocytes and osteoclasts. Matrix consists of collagen fibres, ground substance and also inorganic components. The surface of the bone has coverings of connective tissue known as periosteum and endosteum.

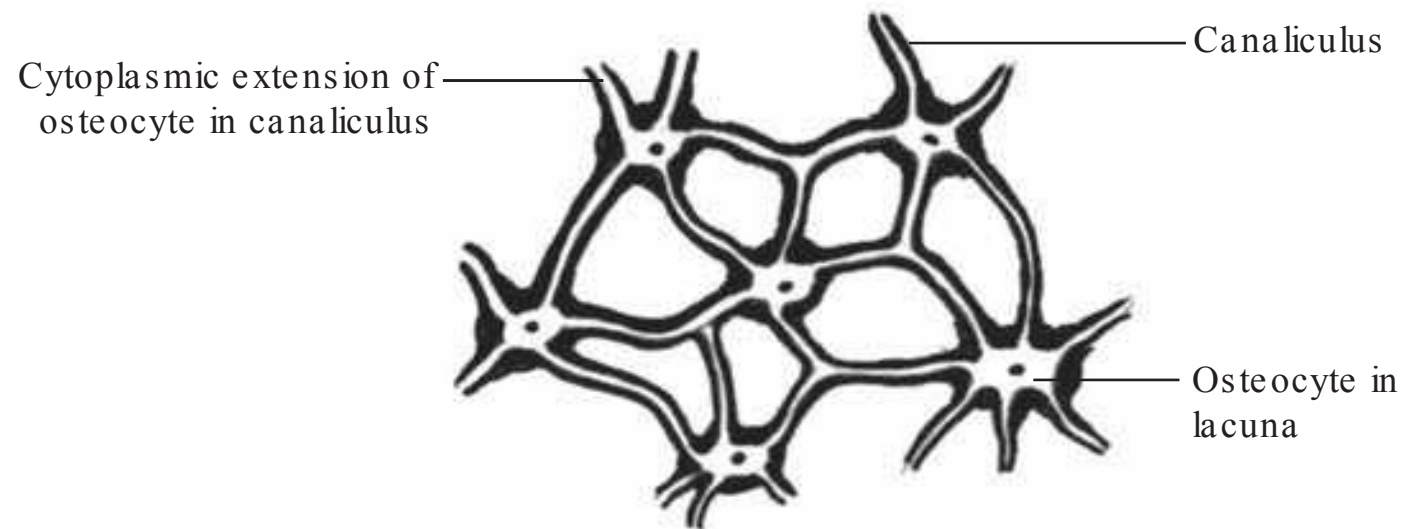
### OSTEOBLASTS

- Osteoblasts are bone-forming cells.
- They are derived from osteoprogenitor cells (which are present in periosteum and endosteum).
- They synthesise organic components of the bone matrix. During the process, they get trapped in the matrix and differentiate into osteocytes.
- They are cuboidal cells, arranged like simple epithelium on the surface where the new bone is formed.
- The nucleus of the osteoblast is eccentrically located, away from its bone-forming surface (see Fig. 7.12).

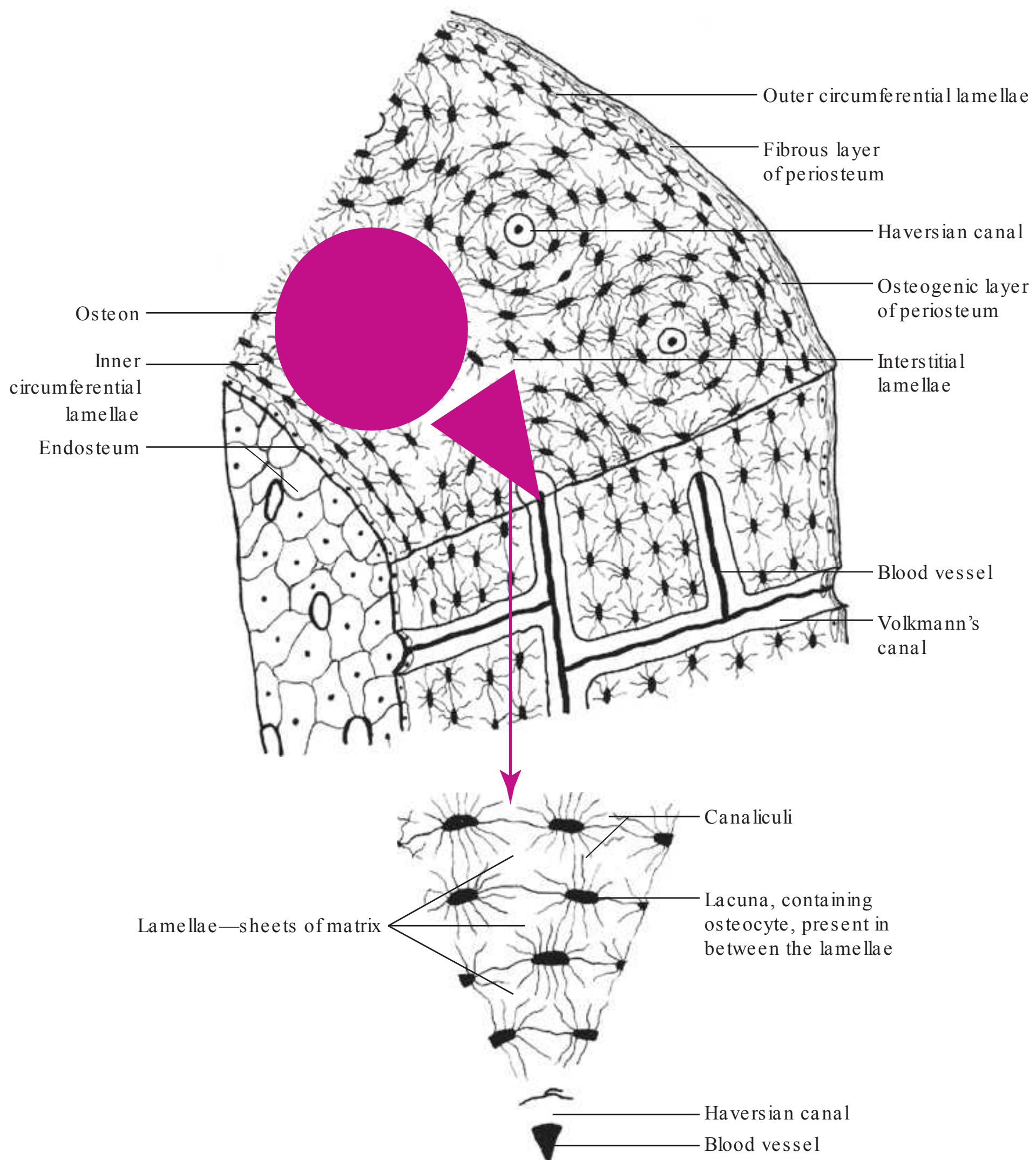
### OSTEOCYTES

- Osteocytes are derived from osteoblasts.
- They are located in the matrix in cavities called lacunae (Figs 7.1 and 7.2; PMG 7.1; see Fig. 7.9), and each lacuna contains a single osteocyte.
- Adjacent lacunae are connected with each other by minute anastomosing canals which pass through calcified matrix. These canals are called canaliculi (singular: canaliculus).
- Within these canaliculi, there are thin cytoplasmic extensions of osteocytes by which the neighbouring osteocytes are in contact with each other through gap junctions (Fig. 7.2). This arrangement helps in exchange of metabolites between blood and the osteocytes.





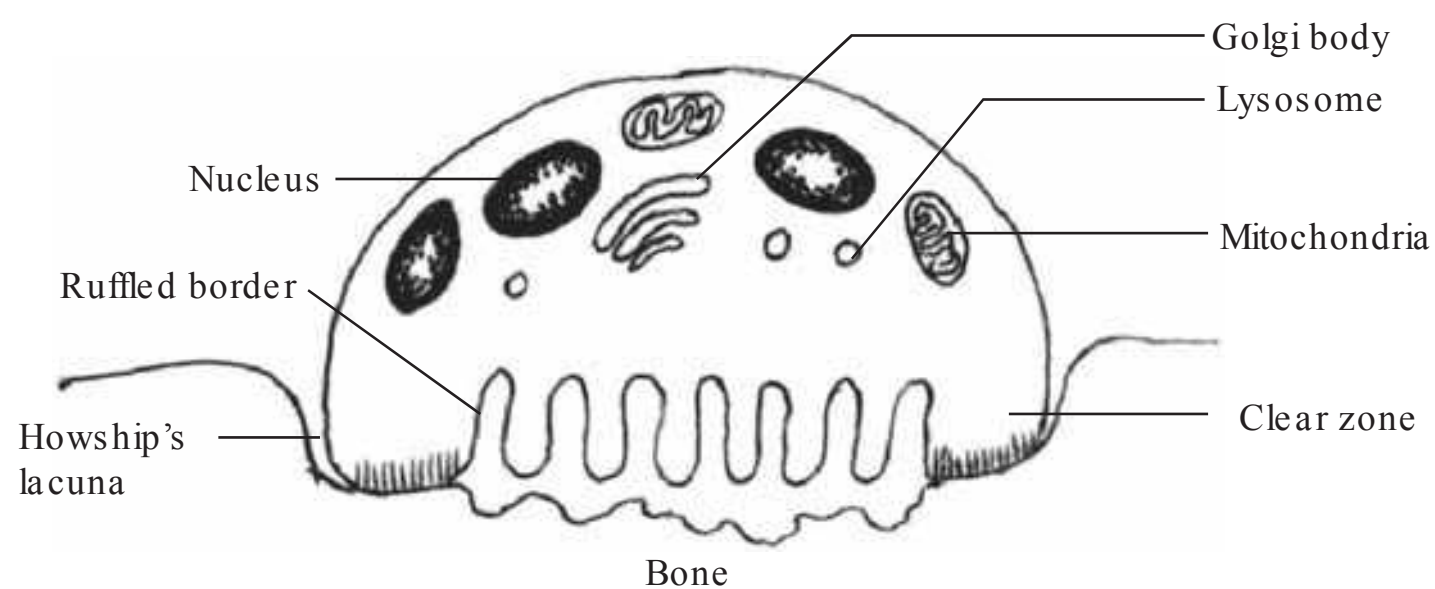
**Figure 7.1** Diagram showing osteocytes. Osteocytes are present inside the lacunae and their cytoplasmic extensions are present within the canaliculi.



**Figure 7.2** Three-dimensional view showing transverse and longitudinal sections of diaphysis of a long bone. Inset shows an enlarged view of part of an osteon in transverse section.

## OSTEOCLASTS

- Osteoclasts are involved in bone resorption.
- These are multinucleated cells derived from the mononuclear phagocyte system.
- They are present in Howship's lacunae (Fig. 7.3; see Fig. 7.12). These lacunae are shallow depressions that are created by osteoclastic activity on the surface of the bone.
- The surface of the osteoclast facing the bone shows a ruffled border. This ruffled border, which facilitates removal of the bony matrix, is characteristic of an active osteoclast. It is formed by the finger-like projections and clefts of the cell membrane (Fig. 7.3).
- The cytoplasm around the ruffled border has very few cell organelles; hence, this region is called a clear zone.
- These cells regulate the blood calcium level under the influence of parathyroid and calcitonin hormones.
- Osteoclasts are stimulated by parathyroid hormone. At the ruffled border, the projections increase in size and bone resorption is increased, which leads to increase in the blood calcium level.
- Calcitonin decreases the activity of the osteoclasts, and the projections at the ruffled border become short or may disappear. Bone resorption is decreased, and therefore the blood calcium level decreases.



**Figure 7.3** Osteoclast.

## BONE MATRIX

- The bone matrix consists of organic and inorganic components.
- Inorganic components are mainly calcium and phosphate. The deposition of these minerals forms hydroxyapatite crystals ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ). These inorganic salts provide hardness to the matrix. Some amount of bicarbonate, citrate, potassium and magnesium are also present in the bone matrix.
- Organic components are type I collagen fibres and ground substance.
- The ground substance is composed of glycosaminoglycans, proteoglycans and some amount of water. Chondroitin sulphate and keratin sulphate are glycosaminoglycans, and osteocalcin and osteopontin are proteoglycans. Proteoglycans bind to calcium, thereby aiding mineralisation of the bone.



## COVERINGS OF THE BONE

The external surface of the bone and the surface facing the marrow cavity (described under 'Long Bone') are covered by layers of connective tissue known as periosteum and endosteum, respectively.

### PERIOSTEUM

- Periosteum is a layer of connective tissue that covers the external surface of the bone, except at the attachment of the muscle.
- It consists of two layers (Fig. 7.2; see Fig. 7.9):
  - (a) The outer layer is the dense connective tissue, consisting of collagen fibres and fibroblasts, and it is called the fibrous layer. Collagen fibres binding the periosteum to the bone are called Sharpey's fibres.
  - (b) The inner layer of periosteum is the osteogenic layer. It has osteoprogenitor cells which have the capacity to divide and differentiate into osteoblasts.

### ENDOSTEUM

- Endosteum lines the inner surface of the bone (the marrow cavity) (Fig. 7.2).
- It is thinner than periosteum.
- It consists of a single layer of osteoprogenitor cells and a small amount of connective tissue.

### FUNCTIONS OF PERIOSTEUM AND ENDOSTEUM

- As mentioned above, endosteum and periosteum contain osteoprogenitor cells. Following injury, these osteoprogenitor cells differentiate into osteoblasts (bone-forming cells) which are involved in the repair of the damaged bone.
- During growth also, osteoprogenitor cells differentiate into osteoblasts.
- Numerous blood vessels enter the bone through the periosteum.

## CLASSIFICATION OF BONE

The human body has more than 200 bones; these have been classified using various parameters. The parameters which are important from the histological aspect are mentioned here.

### 1. Based on their shape and length on gross appearance

- Long (femur, tibia, humerus, etc.)
- Short (carpal and tarsal bones)
- Flat (sternum, scapula and vault of skull)
- Irregular (vertebra, maxilla and temporal bone)

### 2. Based on their gross appearance in a section

- Compact bones
- Spongy bones (described later)

### 3. Based on their histological appearance

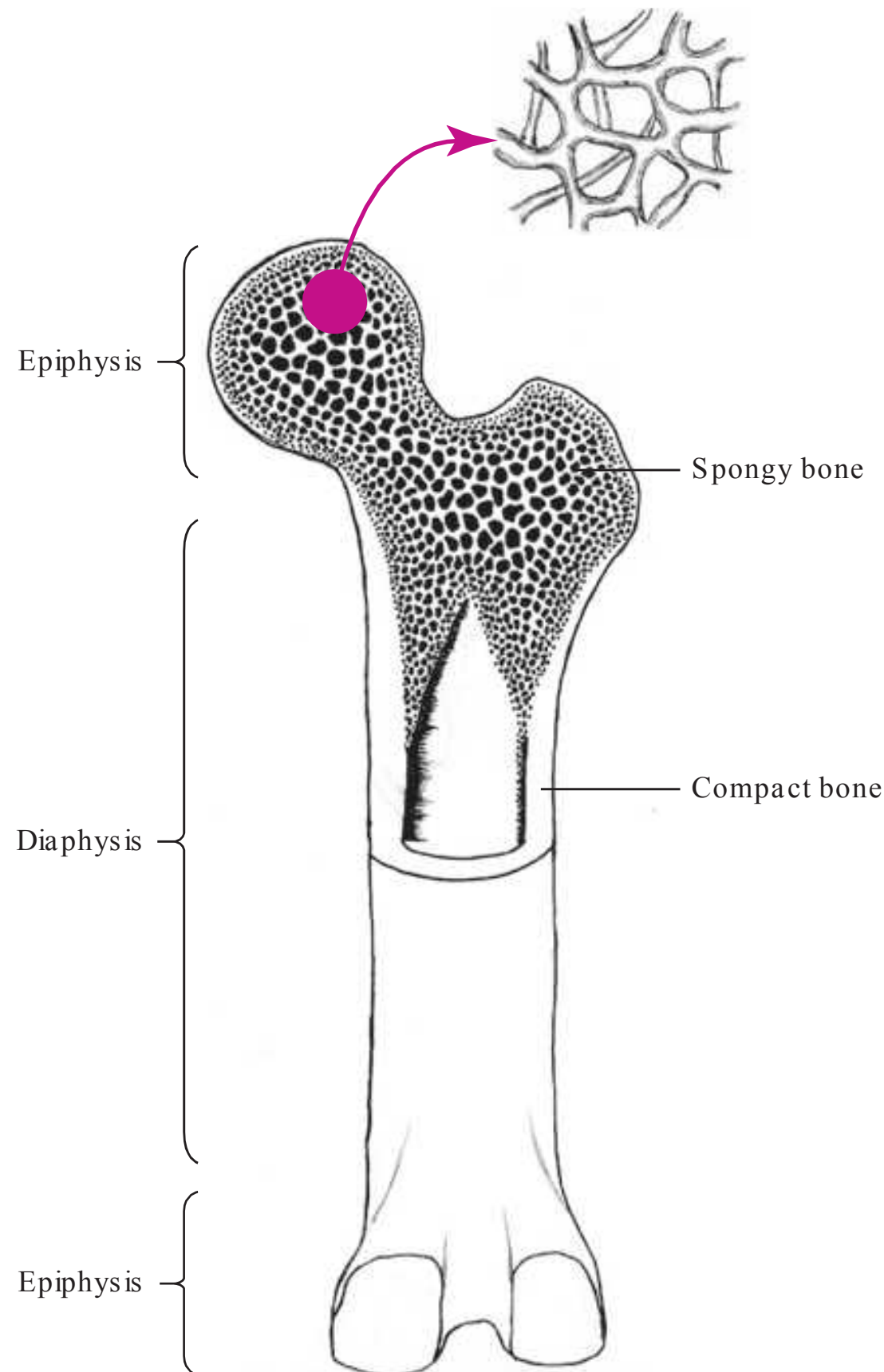
- Woven (immature) bones
- Lamellar (mature) bones (described later)

## LONG BONE

Most of the bones of the limbs (femur, tibia, humerus, etc.) are long bones. The parts of a long bone are discussed in the following text.

### **DIAPHYSES (SINGULAR: DIAPHYSIS)**

- The diaphysis is the long shaft of the bone.
- It is a hollow cylinder composed primarily of compact bones (described later) which surround the medullary cavity (Fig. 7.4).



**Figure 7.4** Gross structure of a long bone. Inset shows the trabeculae of spongy bone.

### **EPIPHYSES (SINGULAR: EPIPHYSIS)**

- The enlarged ends of the long bone are the epiphyses.
- The epiphysis of a bone articulates with the epiphysis of another bone at a joint.
- Most of the epiphysis consists of spongy bones with a thin layer of compact bones overlying it (Fig. 7.4). The articulating surface of the epiphysis is covered by cartilage (usually it is hyaline cartilage; in some joints, e.g. temporomandibular joint, it is covered by fibrocartilage).

### **METAPHYSES (SINGULAR: METAPHYSIS)**

- At the ends of a growing long bone, between epiphysis and diaphysis, there is a band of hyaline cartilage. These bands of cartilage are called the epiphyseal plates. Proliferation of these cartilages is responsible for longitudinal growth of the bone.
- When the growth is completed, epiphyseal cartilage is transformed into bone and forms the metaphyses.



## MEDULLARY CAVITY

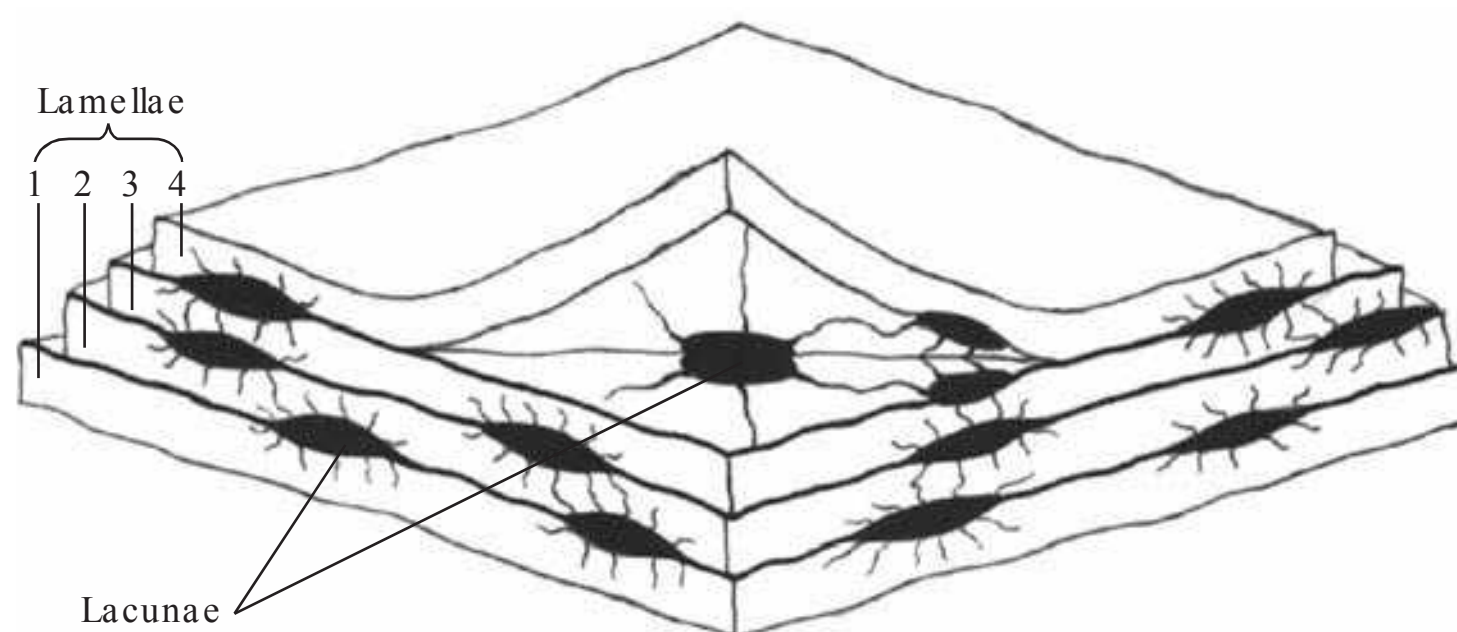
- Medullary cavity is the hollow, central part of the diaphysis (Fig. 7.4).
- In infants, it is filled with red bone marrow. Most of the red bone marrow gets replaced by the yellow bone marrow in adults. The red bone marrow consists of haematopoietic tissue; it gets replaced by fat cells and forms the yellow bone marrow.

## WOVEN (IMMATURE) BONE

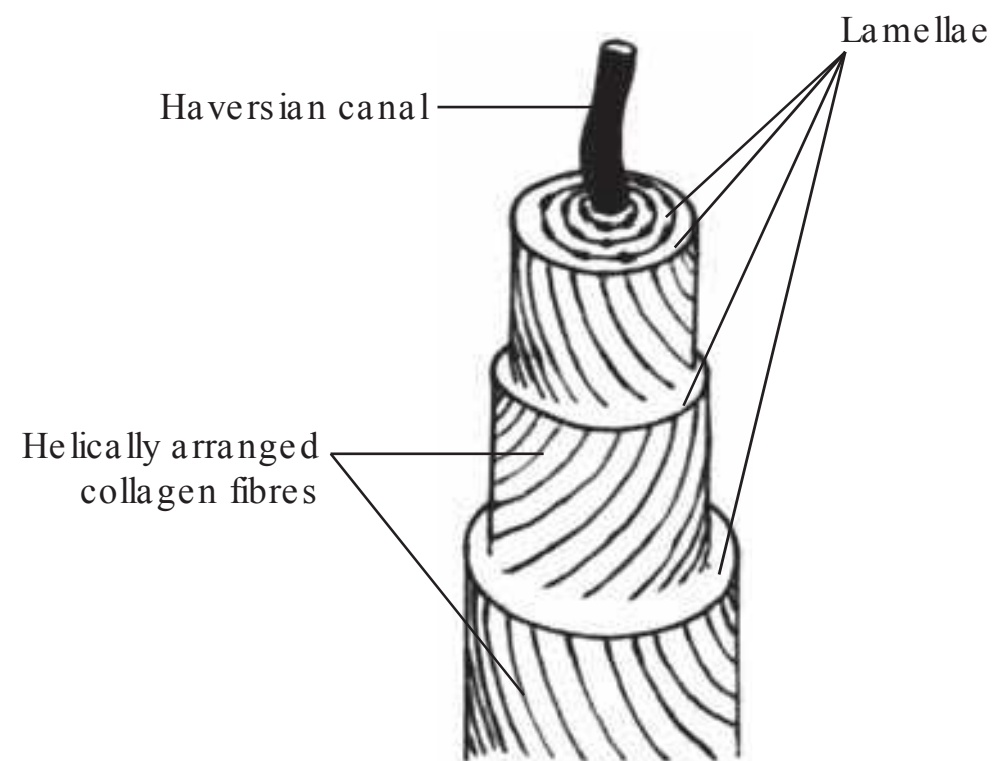
- Woven bone is also known as primary bone.
- It is present in embryonic life and during fracture repair. It is temporary and undergoes remodelling to become lamellar bone.
- It consists of irregularly arranged collagen and osteocytes.

## LAMELLAR (MATURE) BONE

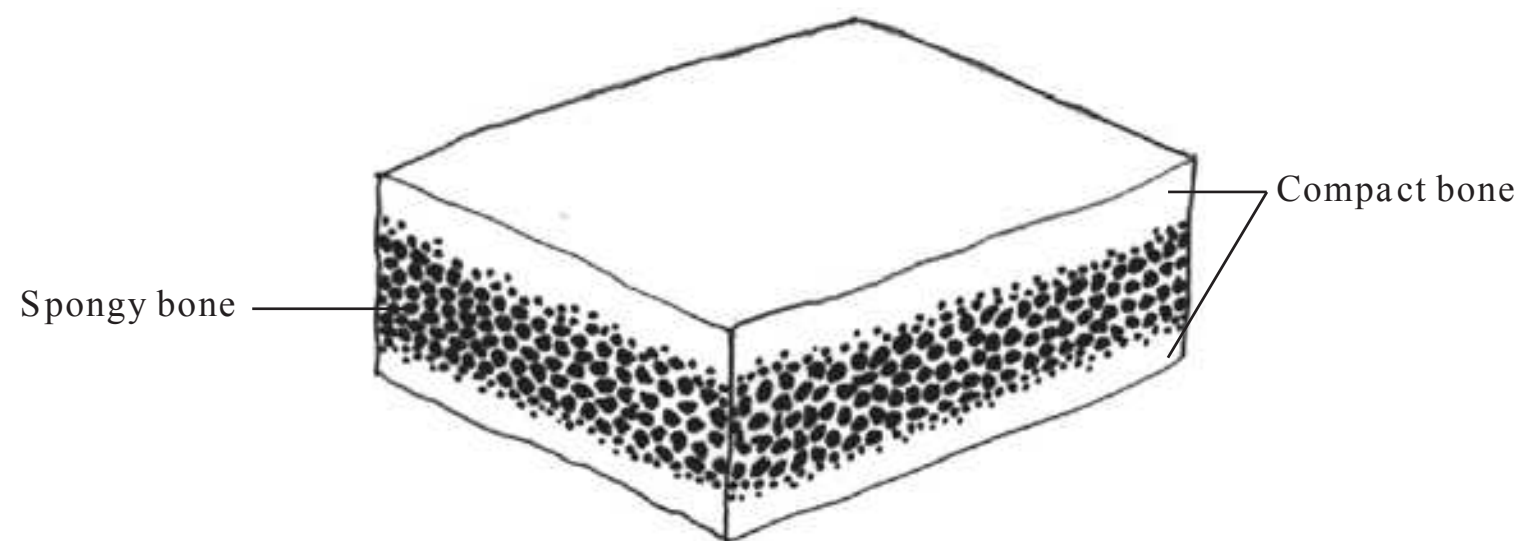
- Lamellar bone is also known as secondary bone.
- The bone matrix is arranged in thin parallel sheets, which are called lamellae (Figs 7.2 and 7.5). Collagen fibres within each lamella run in a helical manner, parallel to each other, around the Haversian canal. The collagen fibres of adjacent lamellae run at right angles to each other (Fig. 7.6). This type of arrangement provides strength to the bone.
- On gross appearance the lamellar bone exists in two forms: compact bone and spongy bone. Epiphyses have spongy bones covered by a thin layer of compact bones (Fig. 7.4). Diaphyses mostly have compact bones; a thin layer of spongy bones is present around the bone marrow (Fig. 7.4). Flat bones have both compact and spongy bones; the compact bone forms the outer and inner plates called tables. The spongy bone sandwiched between the two tables is called diploe (Fig. 7.7). Some examples of flat bones are sternum, scapula and vault of skull.



**Figure 7.5** Lamellar bone—four lamellae (labelled numerically) can be seen. In between the adjacent lamellae, lacunae are present.



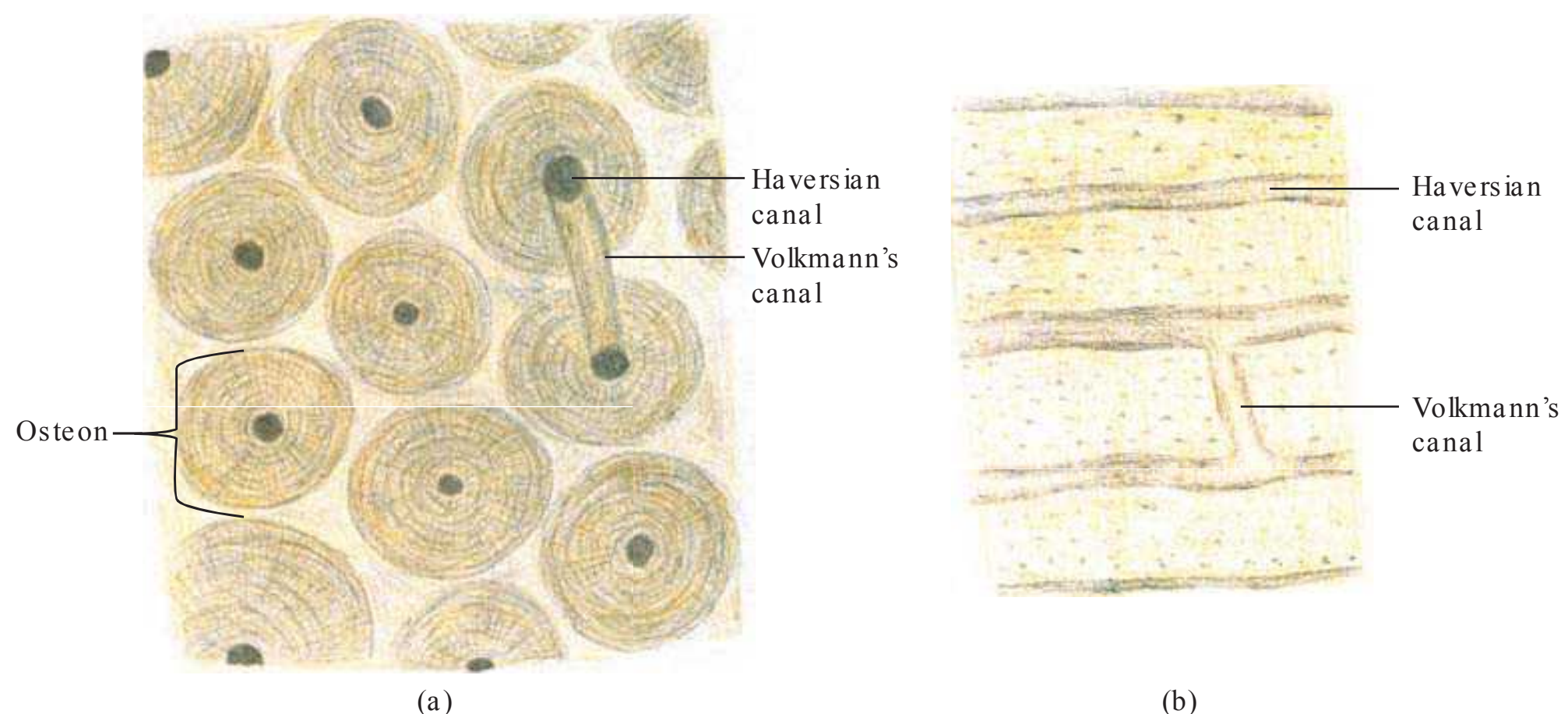
**Figure 7.6** Arrangement of collagen fibres in lamellar bone. (Note that these fibres of adjacent lamellae run at right angles to each other.)



**Figure 7.7** Flat bone.

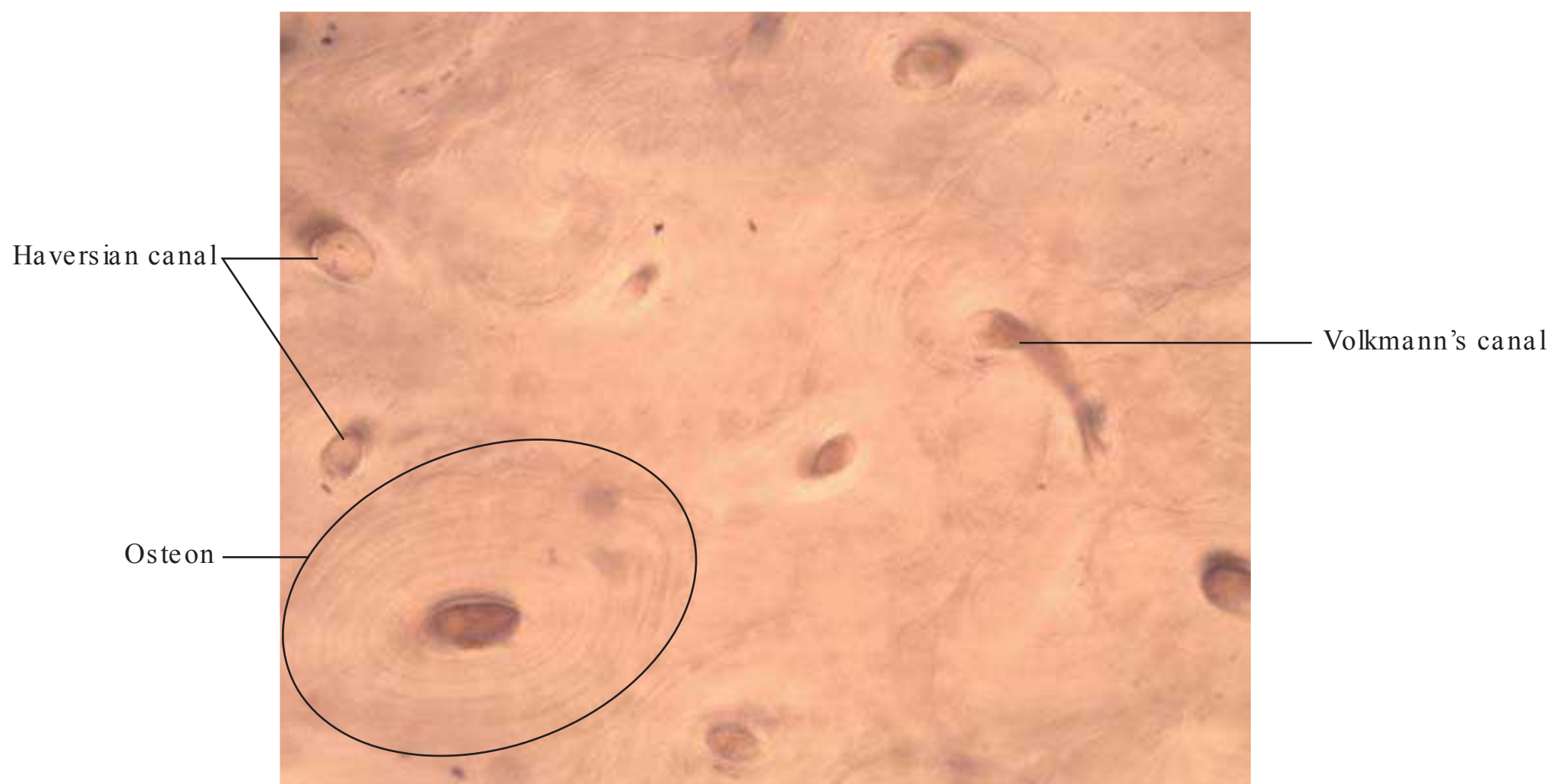
### COMPACT BONE

- The unit of compact bone is Haversian system or osteon. Each osteon consists of a single central canal with its contents, with surrounding lamellae and osteocytes (Fig. 7.8a; PMG 7.1; also see Fig. 7.2 for diagrammatic presentation of structure of osteon).
- Central canal or Haversian canal contains blood vessels, lymphatic vessels and nerves (Fig. 7.8; PMG 7.1 and 7.2). Haversian canal of one osteon is connected to that of another osteon by Volkmann's canal (Fig. 7.8; PMG 7.1), which also connects the periosteum and endosteum.

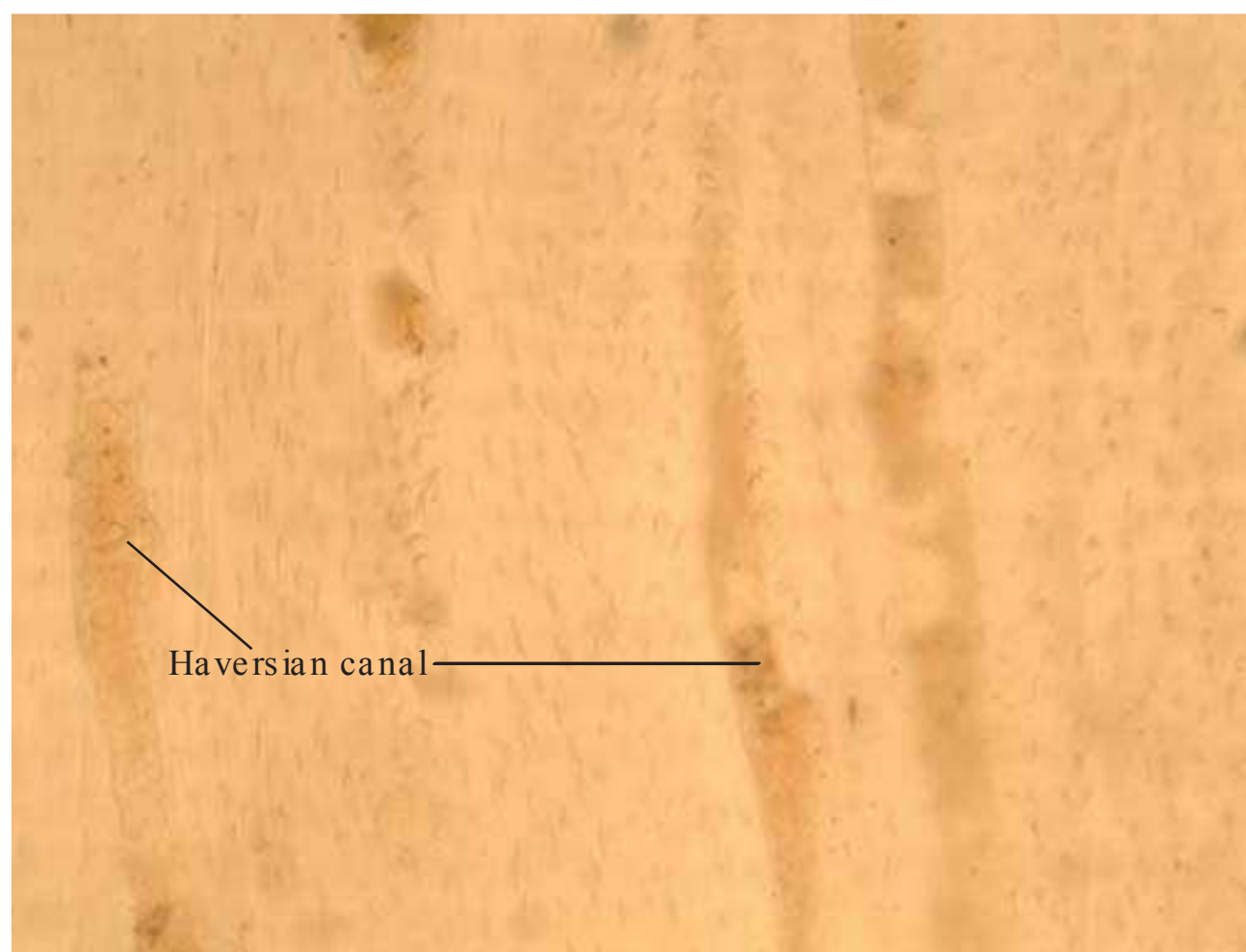


**Figure 7.8** Ground sections of compact bone: (a) transverse and (b) longitudinal sections (drawing).





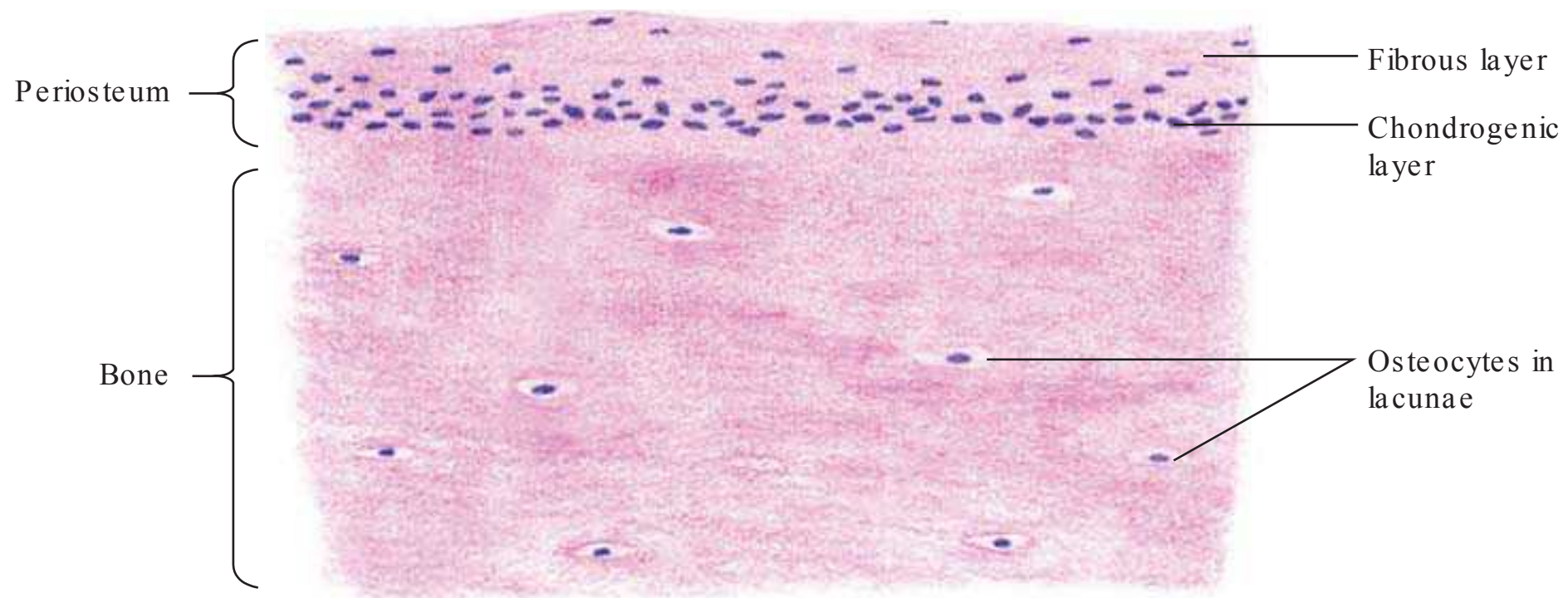
**PMG 7.1** Transverse section of the compact bone (ground section, X10).



**PMG 7.2** Longitudinal section of the compact bone (ground section, X10).

- Lamellae (singular: lamella) are thin sheets of the bony matrix arranged concentrically around the central canal. Based on their location within the bone, lamellae can be classified as follows (Fig. 7.2):
  - (a) Inner circumferential lamellae: Present around the marrow cavity over the endosteum
  - (b) Outer circumferential lamellae: Present beneath the periosteum
  - (c) Interstitial lamellae: Present in between the osteons. These are remnants of osteons that were partially resorbed during the process of bone remodelling (described under 'Ossification').
- Osteocytes are present in lacunae which lie between the lamellae (Fig. 7.9). As described earlier, adjacent lacunae are connected with each other by their canaliculi. Within these canaliculi, there are cytoplasmic extensions of osteocytes by which the neighbouring osteocytes are in contact with each other. This network of canaliculi facilitates the diffusion of nutrients and metabolites between osteocytes and blood capillaries.
- A thin line that marks the boundaries between adjacent osteons is called cement line. These lines are formed as a result of the bone remodelling process.

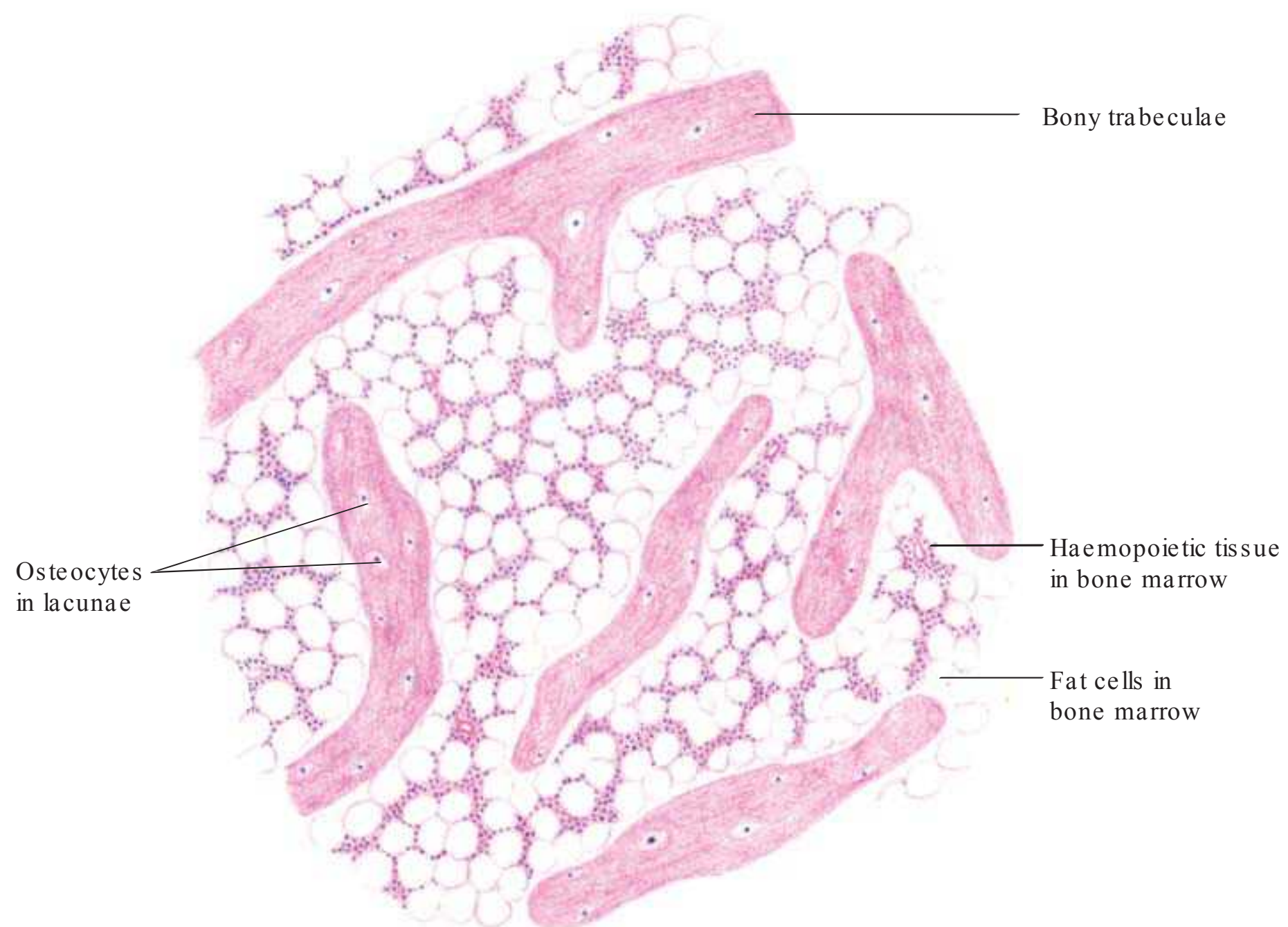




**Figure 7.9** Section of a compact bone in low magnification (H&E pencil drawing).

### **SPONGY BONE**

- Spongy bone is also called cancellous bone.
- It consists of a network of thin irregular bars of bone called trabeculae (singular: trabecula), separated by interconnecting spaces, resembling a sponge (Figs 7.4 and 7.10). These small spaces around the trabeculae contain the bone marrow.
- It does not have the Haversian system.
- Osteocytes, lacunae and canaliculi in the trabecular bone resemble those in the compact bone.
- Osteocytes get nutrition through canaliculi, which communicate with blood sinusoids present in the bone marrow.



**Figure 7.10** Section of a spongy bone in low magnification. A network of bony trabeculae separated by interconnecting spaces (containing bone marrow) can be seen (H&E pencil drawing).

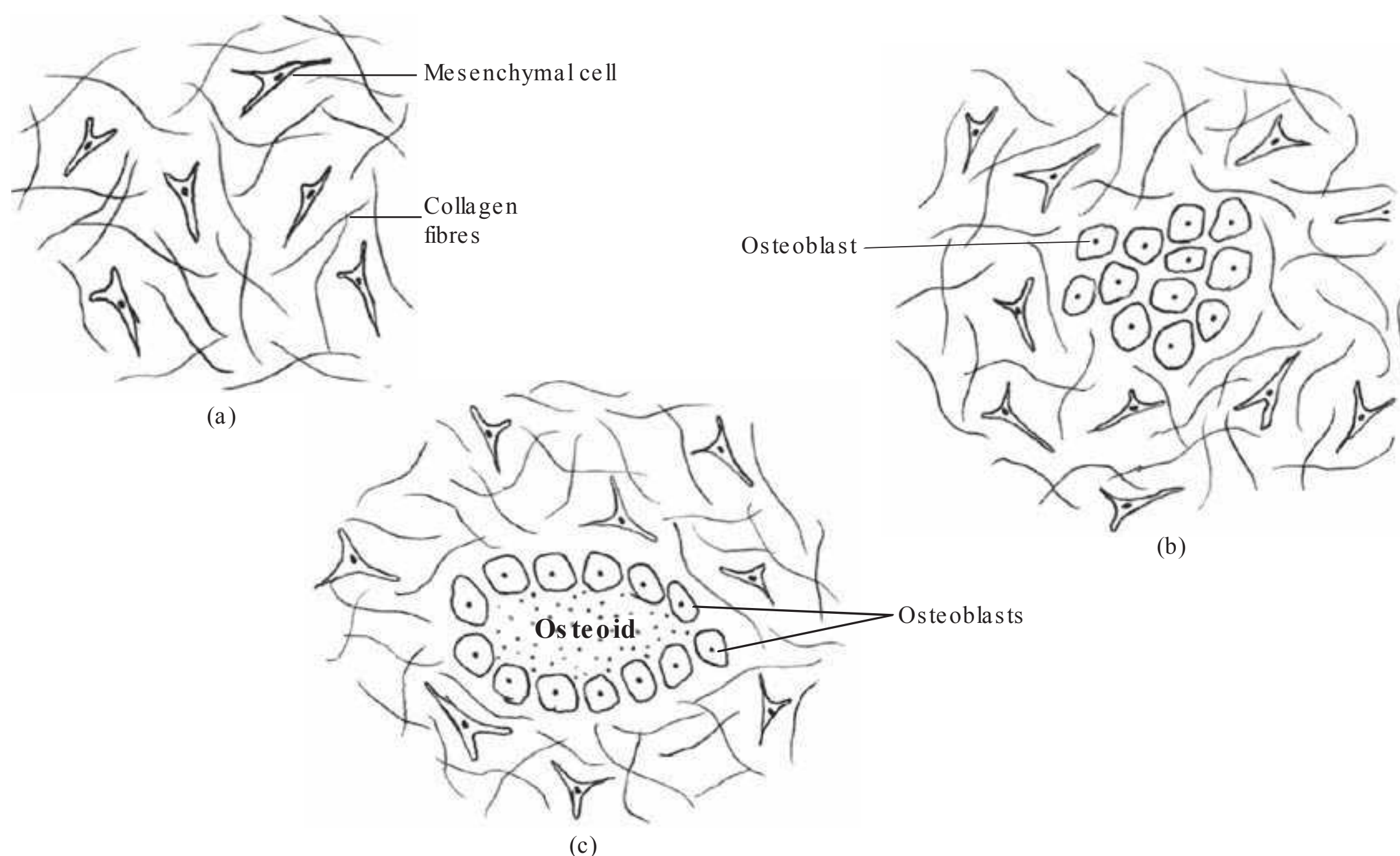


## OSSIFICATION

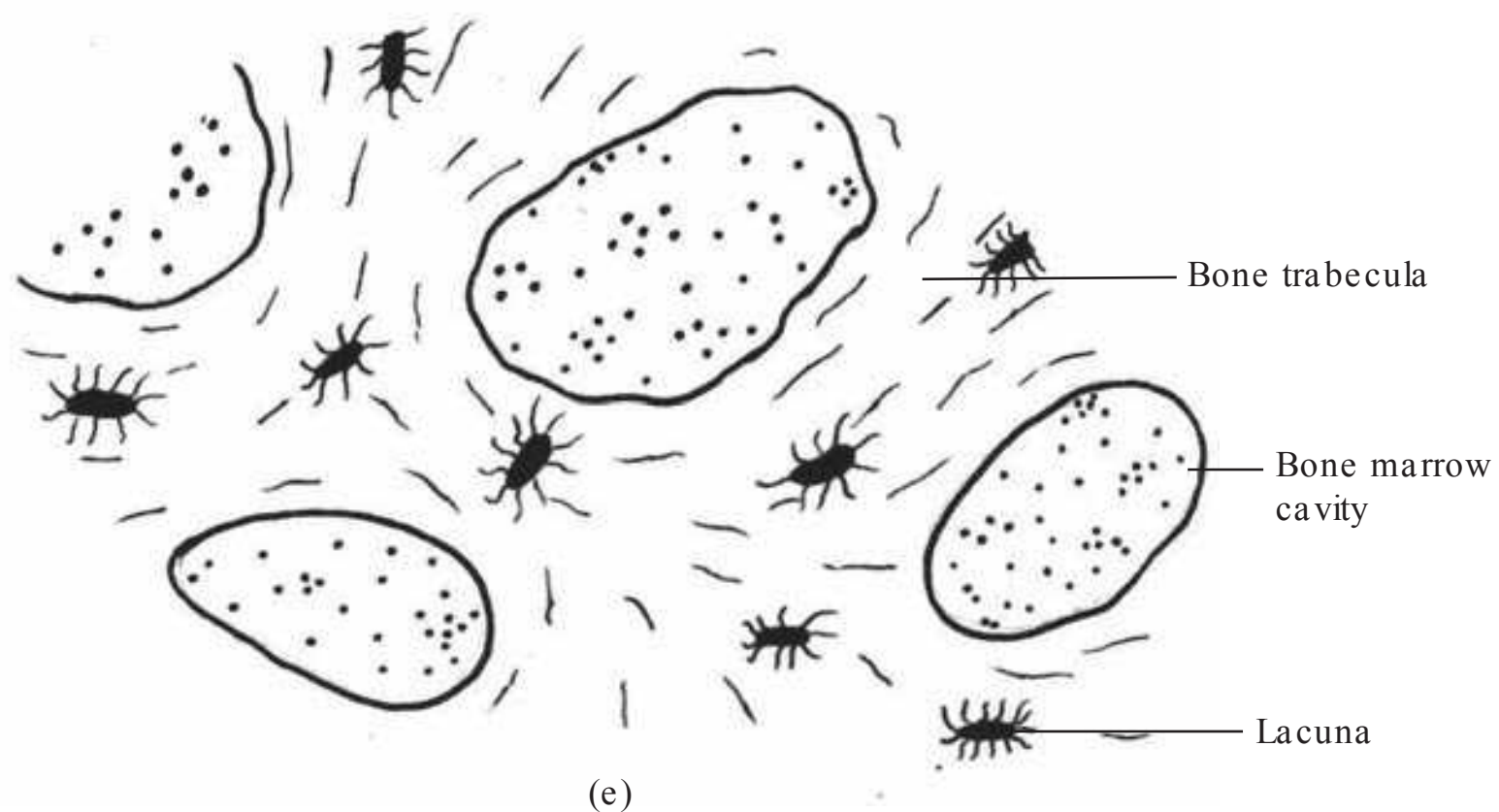
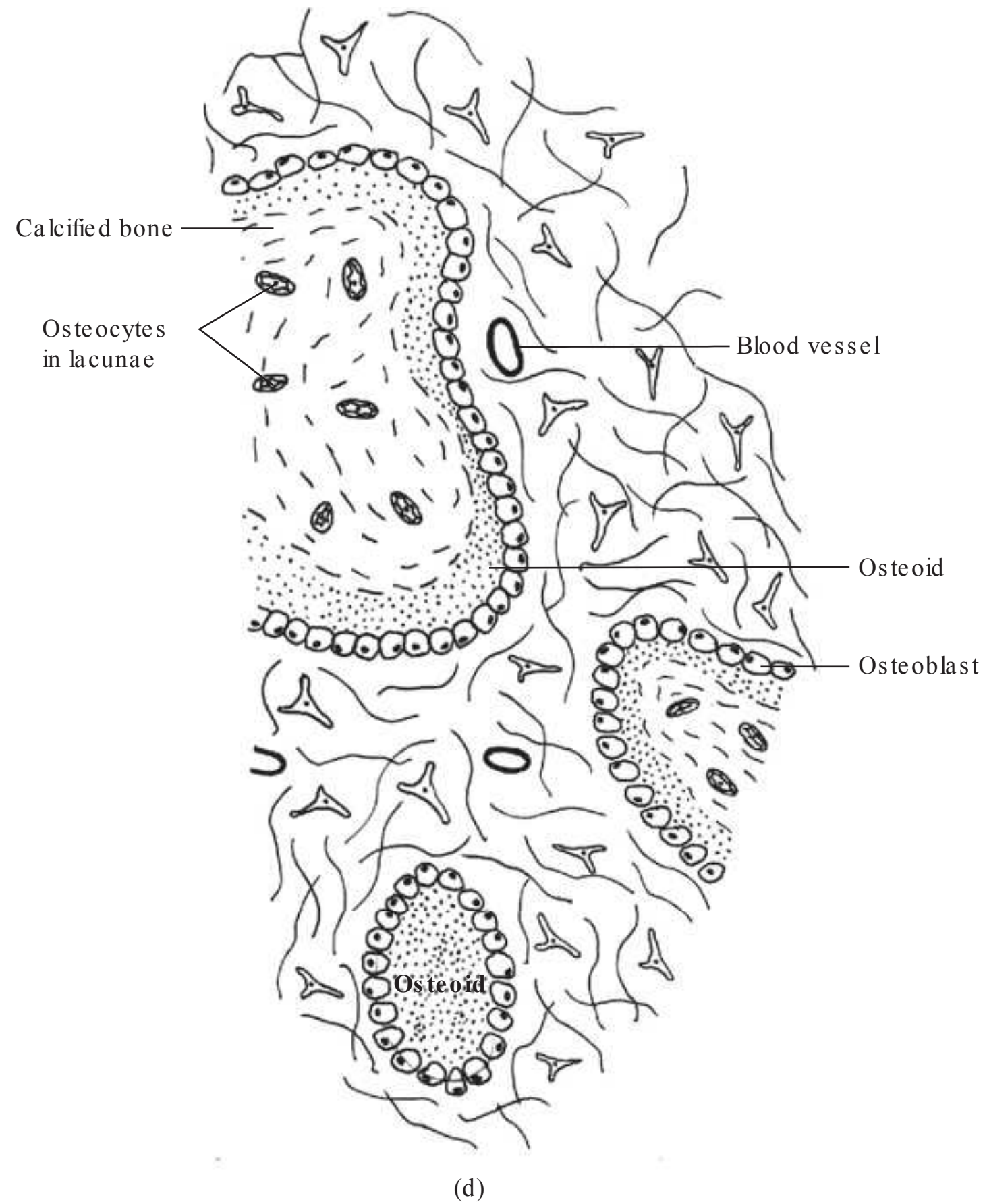
- Ossification is the process of bone formation.
- The bone is formed by two processes: intramembranous and endochondral ossification.
- In intramembranous ossification, the bone is formed directly in a primitive connective tissue.
- In endochondral ossification, the bone is formed in the preformed cartilage model (endo means 'within' and chondro means 'cartilage').

### INTRAMEMBRANOUS OSSIFICATION

- Intramembranous ossification gives rise to flat bones of skull.
- In the areas where the bone is to form, mesenchymal cells (Fig. 7.11a and b) differentiate into osteoprogenitor cells, and these cells give rise to osteoblasts. Areas where these changes occur are called ossification centres (Fig. 7.11b).
- Osteoblasts lay down matrix, and this newly formed unmineralised matrix is called osteoid (Fig. 7.11c).
- As more and more matrix is deposited, some of the osteoblasts become entrapped in the lacuna of the matrix and their processes get entrapped in the canaliculi (Fig. 7.11d).
- On the surface of the centre of ossification, new osteoblasts are formed from differentiation of osteoprogenitor cells, which lay down more osteoid.
- There are several centres of ossification throughout the mesenchymal tissue (Fig. 7.11d). As more bone is formed, these centres fuse with each other and result in the formation of scattered, irregular trabeculae. The fusion of trabeculae gives rise to spongy bone (Figs 7.11e and 7.12).
- In the newly formed bone, collagen fibres are arranged randomly, and the bone is called woven bone. Later this bone is replaced by the lamellar bone after remodelling (described later).



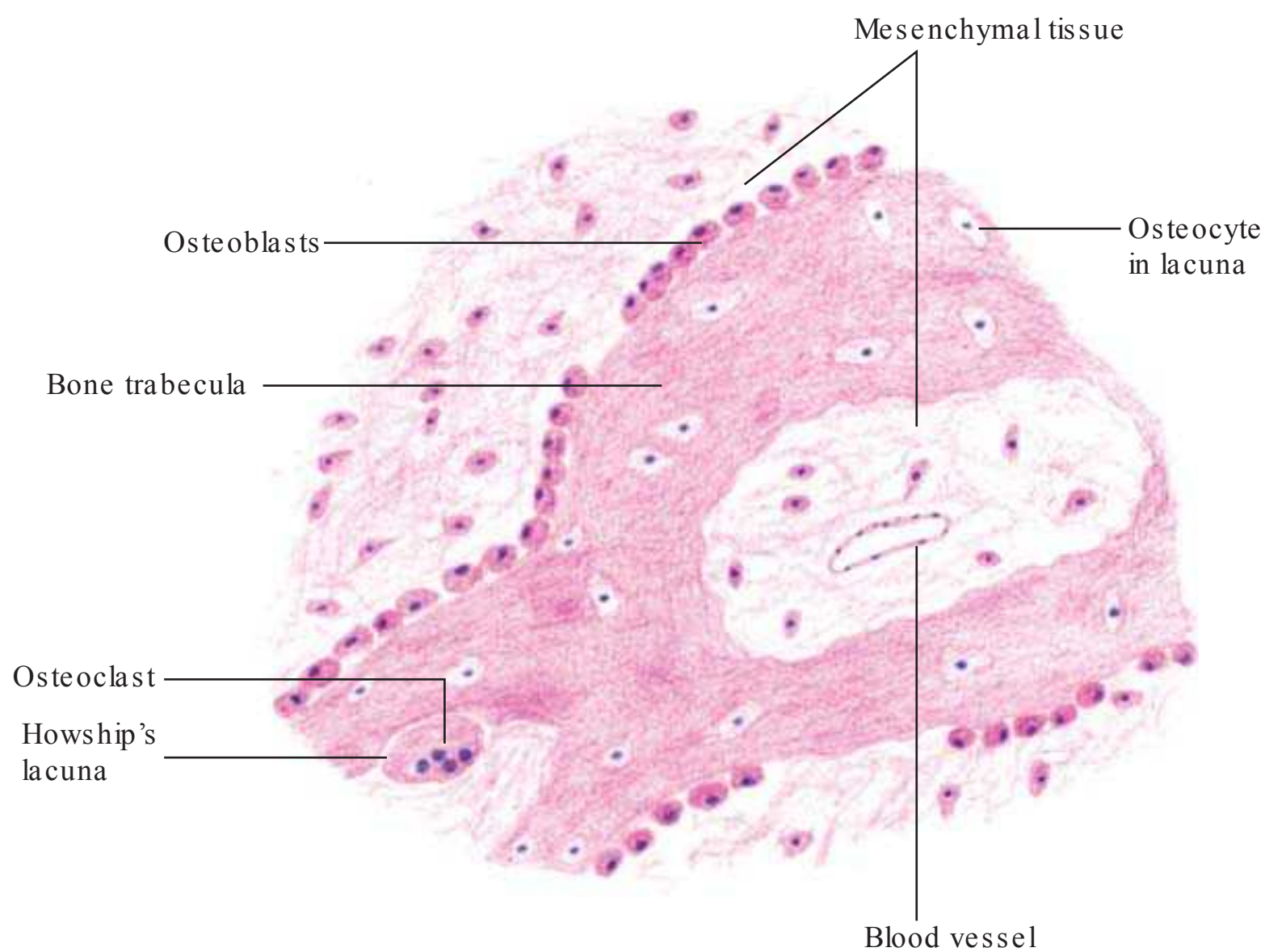
**Figure 7.11a–e** Steps of intramembranous ossification. (a) Mesenchymal tissue. (b) Mesenchymal cells differentiate into osteoblasts—the cluster of osteoblasts forms the ossification centre. (c) Osteoblasts begin to secrete osteoid. (continued)



**Figure 7.11** (continued) (d) Diagram showing three ossification centres. As more bone is formed, these centres fuse with each other and result in the formation of scattered, irregular trabeculae. The fusion of trabeculae gives rise to spongy bones. (e) Spongy bone, consisting of a network of bony trabeculae separated by interconnecting spaces containing the bone marrow.



- The mesenchymal tissue intervening between the trabeculae of spongy bone gets vascularised and differentiates into the bone marrow (Figs 7.11e and 7.12).
- As new bone is added on the surface of the trabeculae (appositional growth), the spaces between them are narrowed and eventually get obliterated and the bone becomes compact bone. This compact bone forms the inner and outer tables of skull bone.
- The connective tissue surrounding the developing flat bone, which does not undergo ossification, forms the periosteum and endosteum.



**Figure 7.12** Section of bone showing intramembranous ossification. Osteoblasts deposit new bone on one side of a bony trabecula, while osteoclasts sitting in the Howship's lacunae resorb on the other side (H&E pencil drawing).

## ENDOCHONDRAL OSSIFICATION

Endochondral ossification begins in the hyaline cartilage and gives rise to long bones.

### **Formation of Primary Areolae**

- In the hyaline cartilage, towards the centre of the shaft, chondrocytes enlarge and mature (Fig. 7.13a and b).
- The matrix surrounding these mature chondrocytes undergoes calcification (Fig. 7.13b).
- Nutrients cannot diffuse through the calcified matrix, and this leads to the death of chondrocytes.
- The death of enlarged chondrocytes produces large spaces, which are called primary areolae (Fig. 7.13c).

### **Formation of Periosteal Collar**

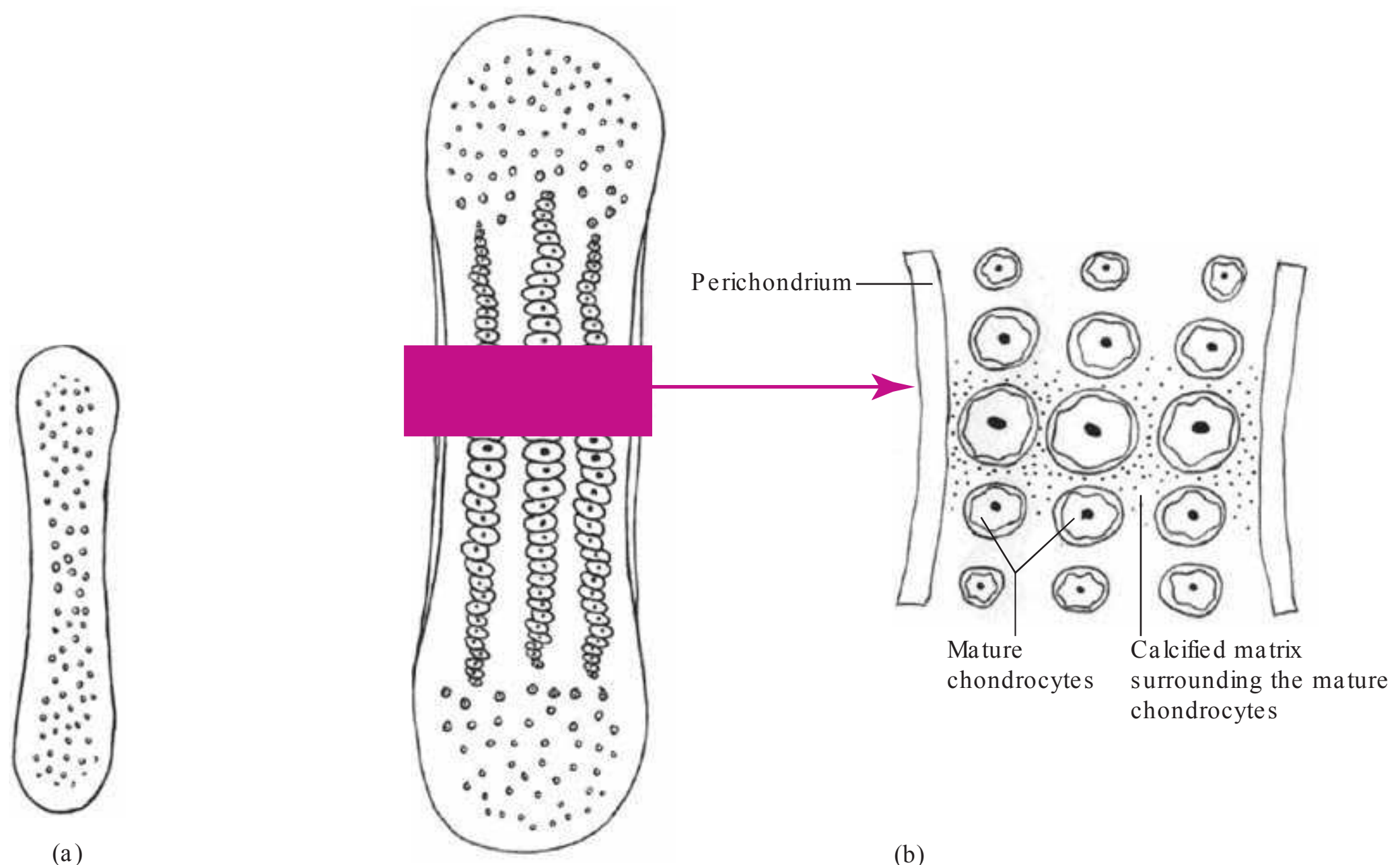
- As these changes occur, simultaneously the perichondrium develops osteogenic potential. The perichondrium is vascularised and chondrogenic cells become osteoprogenitor cells.
- Osteoprogenitor cells differentiate into osteoblasts, and at this stage the perichondrium is transformed into periosteum.
- Osteoblasts lay down a thin layer of bone underneath the periosteum on the surface of the shaft and form a periosteal bone collar (Fig. 7.13c).

### Formation of Primary Centre of Ossification

- Osteoprogenitor cells of perichondrium form periosteal bud, which consists of blood capillaries, osteoprogenitor cells and osteoclasts (Fig. 7.13d).
- The periosteal bud excavates through the bone collar and erodes the wall of primary areolae; the primary areolae fuse and form larger spaces known as secondary areolae (Fig. 7.13e).
- The space gets filled with primitive bone marrow cells.
- Osteoblasts form osteoid on the surface of the calcified cartilage matrix, and the osteoid gets calcified, forming trabeculae of spongy bone. Later, the calcified cartilage matrix present in the core of the trabeculae is removed by osteoclasts, giving rise to mature trabeculae of the spongy bone.
- The central part of the cartilage model where these changes occur is now called the primary centre of ossification (Fig. 7.13e).
- Similar processes occur in the cartilage close to the shaft, resulting in formation of bone towards the epiphysis.

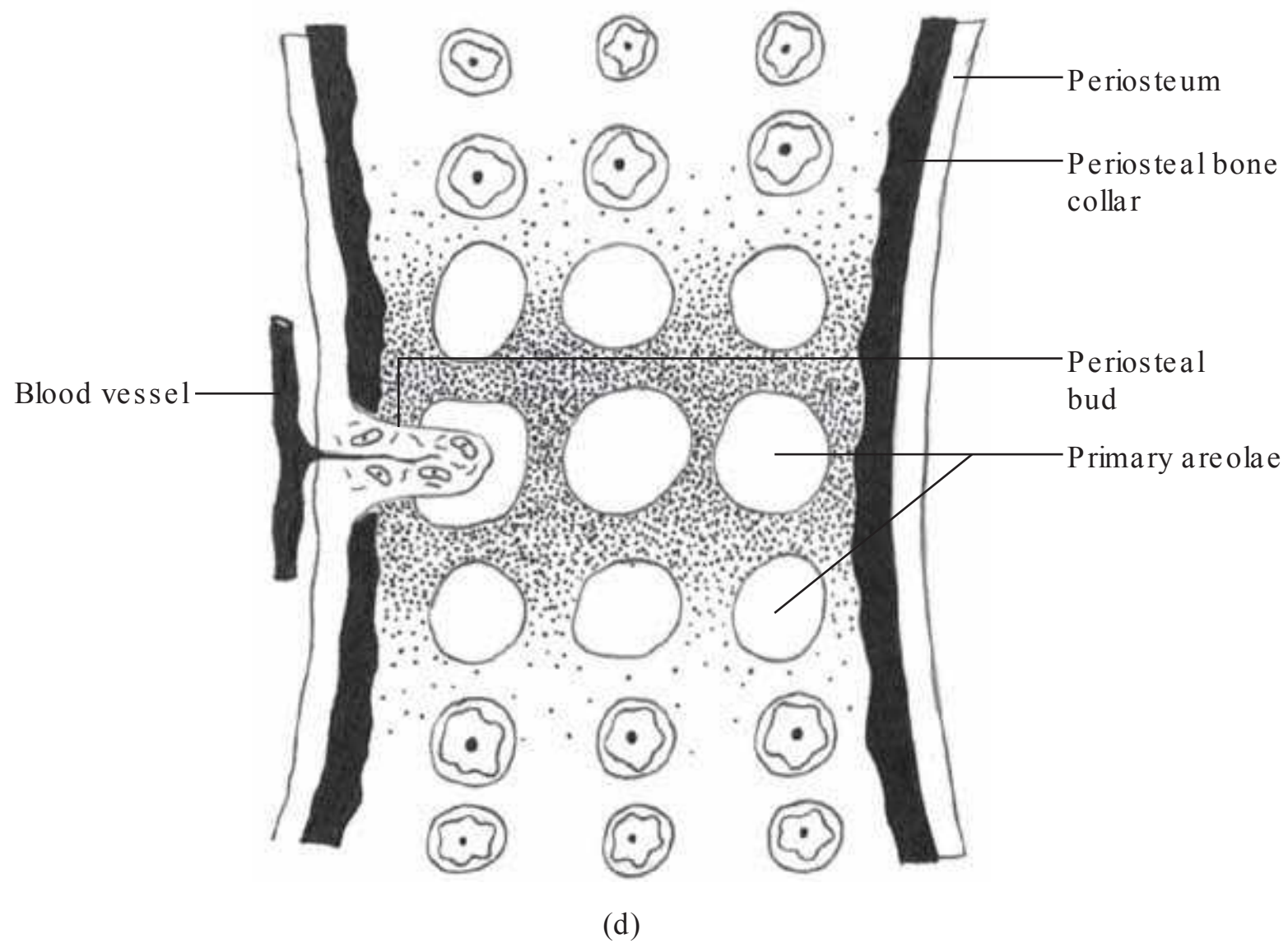
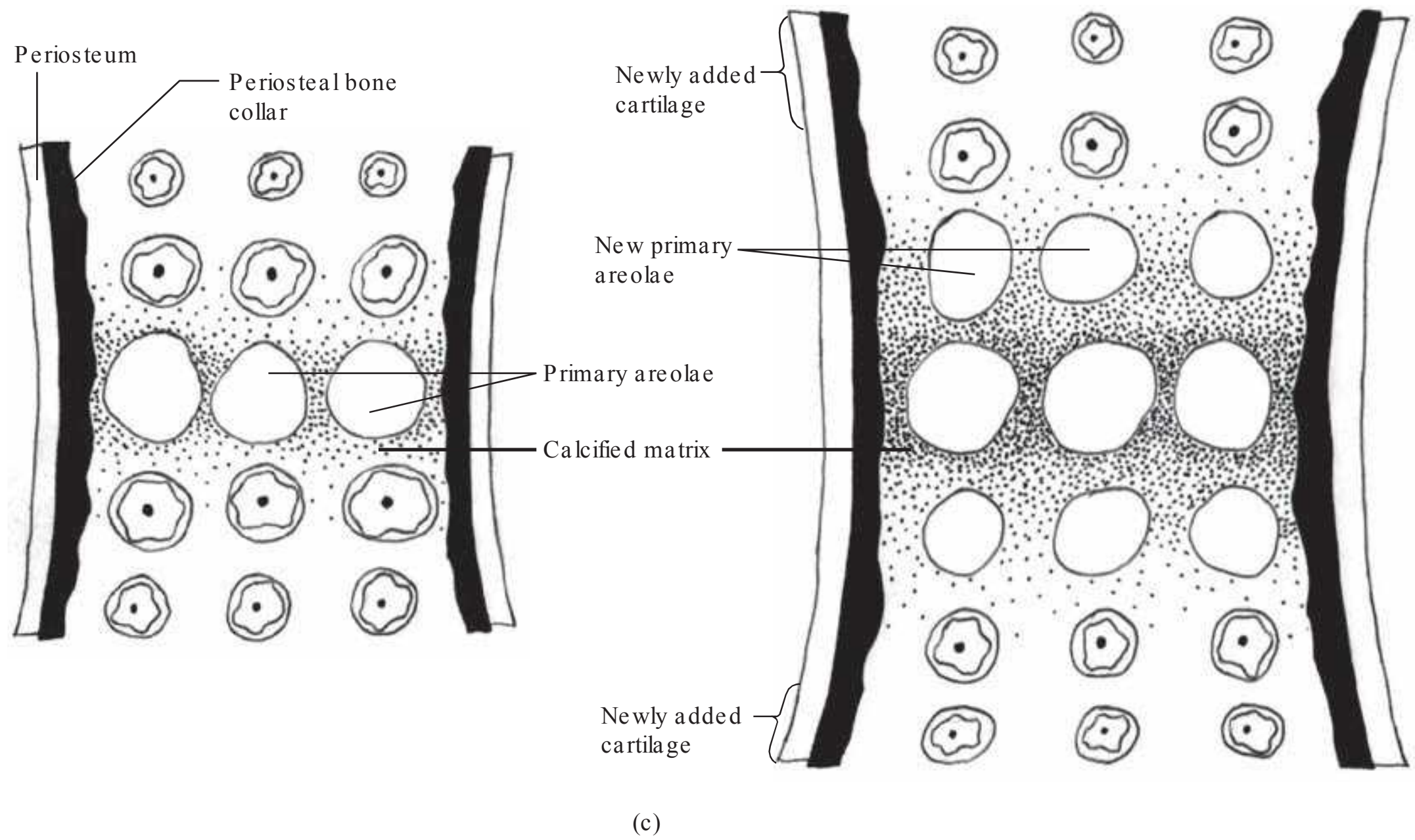
### Secondary Centres of Ossification

- After birth, new centres of ossification, secondary ossification centres, appear in the ends of long bones (Fig. 7.13f).
- The cartilage of the epiphyses undergoes the same sequence of events as in the diaphysis. In the secondary centre, the cartilage growth and subsequent ossification spreads out in all directions (Fig. 7.13f).
- Entire cartilage is replaced by bone except in two regions: at the free end, which remains as articular cartilage, and between the epiphysis and the diaphysis, forming the epiphyseal plate or epiphyseal cartilage.

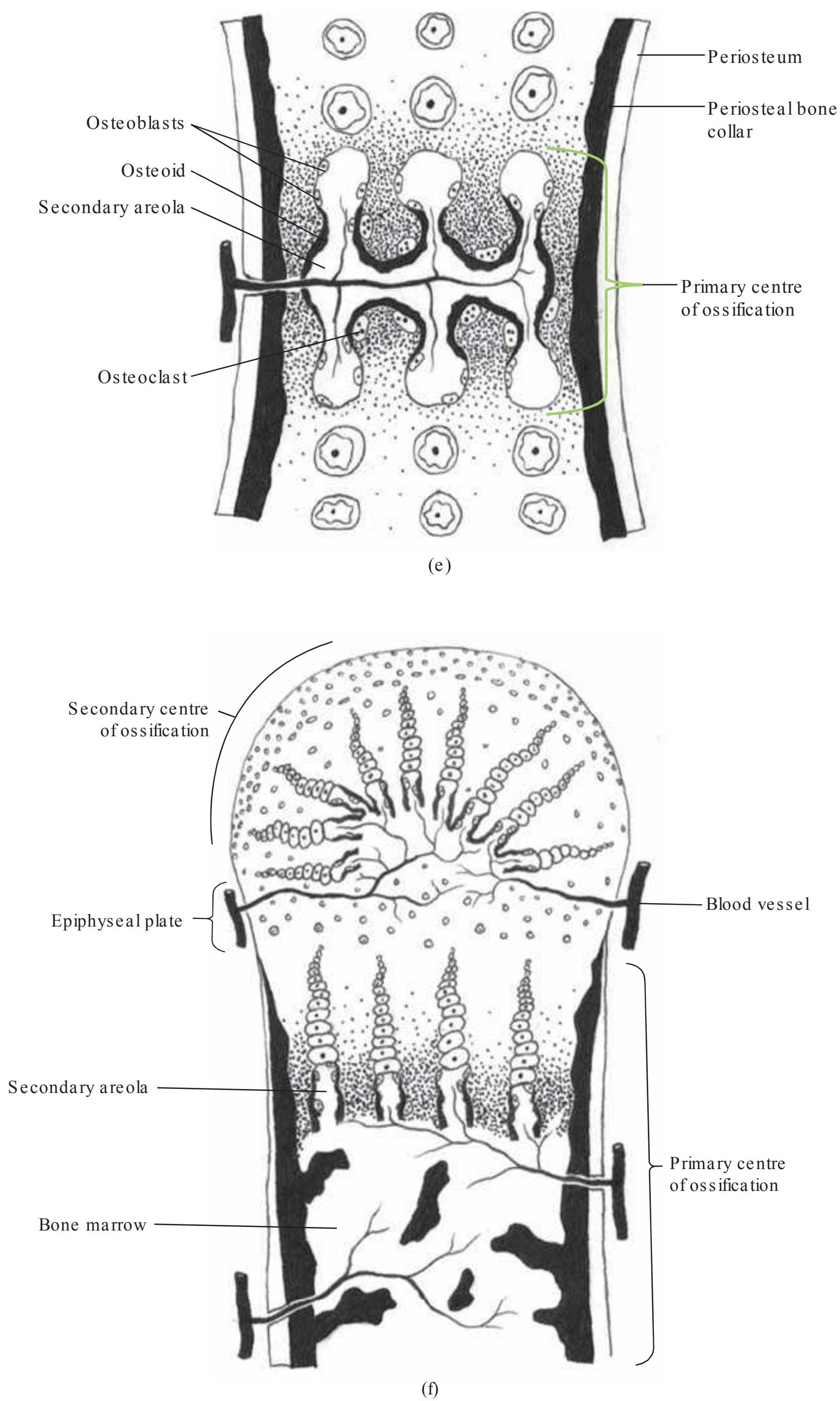


**Figure 7.13a–g** Steps of endochondral ossification. (a) Longitudinal section of a growing hyaline cartilage. (b) As cartilage increases in size, chondrocytes mature and enlarge towards the centre of the shaft. (continued)



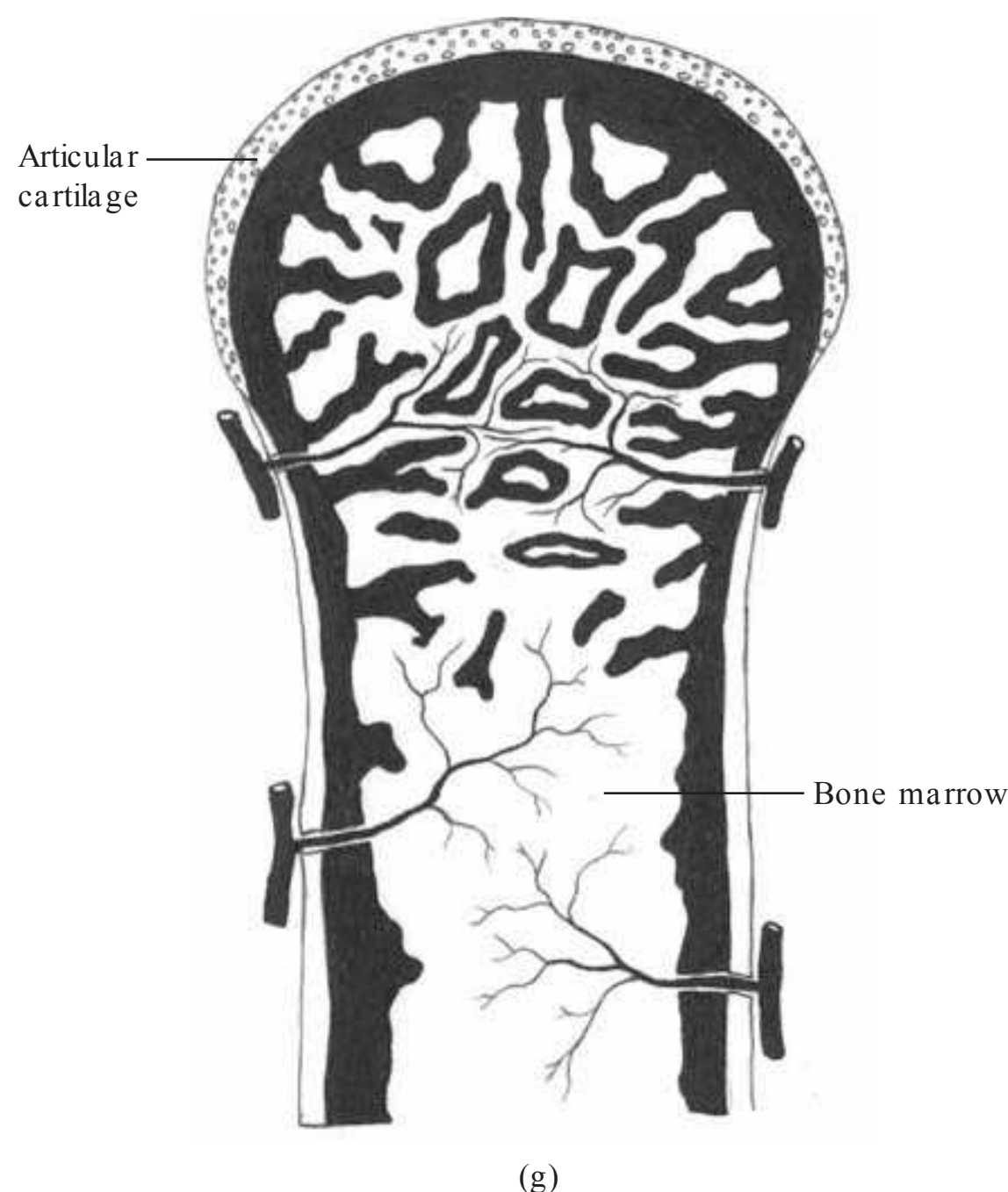


**Figure 7.13** (continued) (c) Formation of periosteal bone collar and primary areolae. On the right side, note the newly formed cartilage at both ends as cartilage continues to grow in length. (d) Periosteal bud eroding the wall of primary areola. (continued)



**Figure 7.13** (continued) (e) The primary centre of ossification. (f) Diagram showing expanding bone marrow and appearance of the secondary ossification centre. (continued)



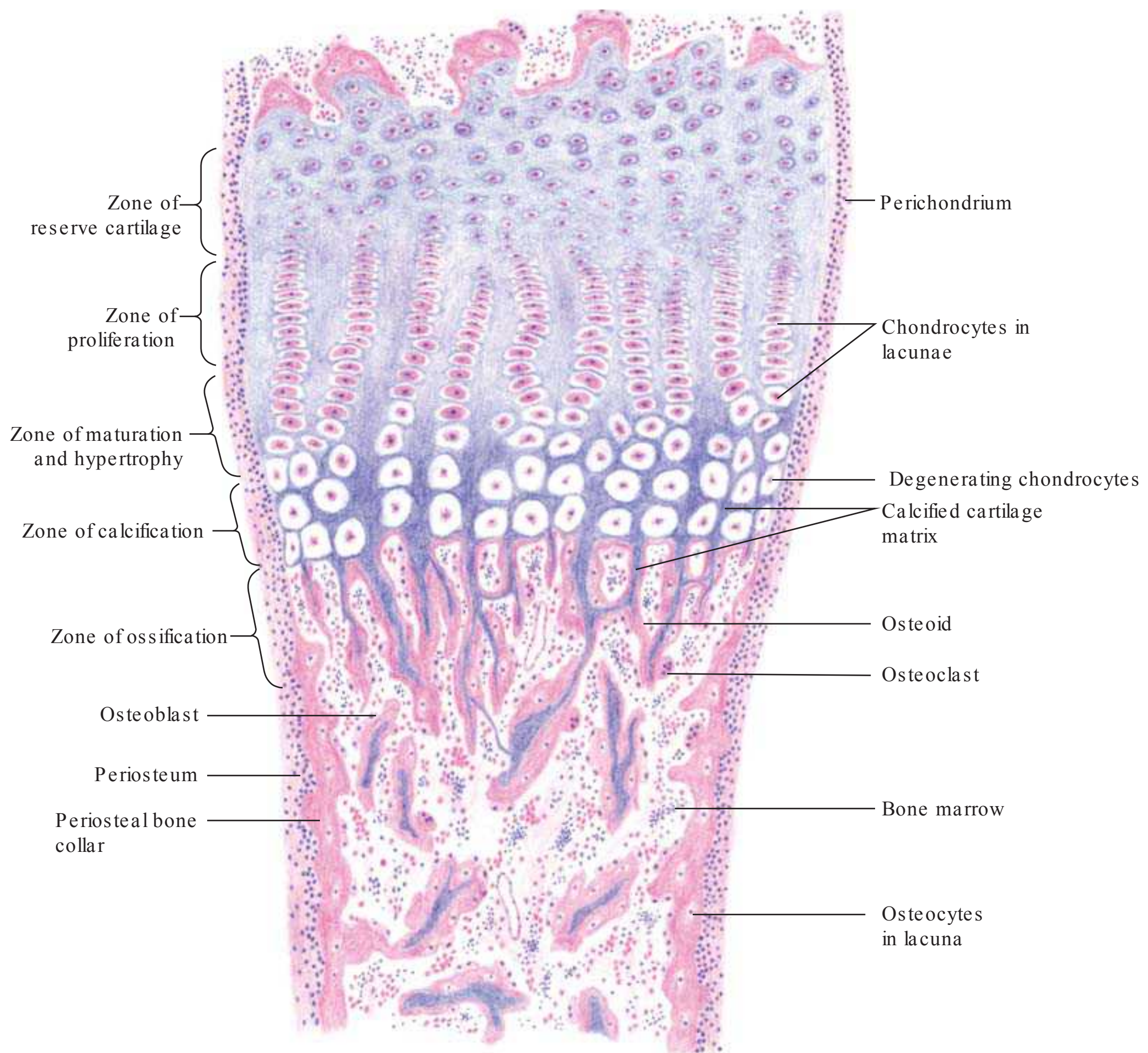


**Figure 7.13** (continued) (g) Fusion of epiphysis, causing cessation of growth.

### Epiphyseal Plate

- In most of the bones, the primary and secondary ossification centres do not fuse before adulthood.
- The bone continues to grow in length till adulthood due to proliferation of cartilage of the epiphyseal plate.
- The cells in the epiphyseal cartilage proliferate, and new cartilage is added at the metaphyseal ends of the diaphysis of the growing bone.
- As the new cartilage is added at both ends of diaphysis, the growing bone increases in length, and as a result, the two epiphyseal plates move apart (see Fig. 7.16). Later, the newly formed cartilage gets ossified (see Fig. 7.16).
- When the growth is complete, the cartilage of the epiphyseal plate is transformed into bone, and the epiphysis fuses with the diaphysis (Fig. 7.13g; also see Fig. 7.16).
- In the growing bone, the epiphyseal cartilage shows the following zones of activity (Fig. 7.14):
  - (a) Zone of reserve cartilage: This zone appears like a mature hyaline cartilage. Chondrocytes are randomly distributed throughout the matrix. This zone is closest to the epiphysis and furthest away from the primary centre of ossification.
  - (b) Zone of proliferation: In this region, chondrocytes divide mitotically and form rows of chondrocytes separated by a small amount of matrix.
  - (c) Zone of maturation and hypertrophy: The cells in this zone do not divide; they mature and enlarge in size. The lacunae also increase in size; as a result, the matrix between the rows of chondrocytes becomes thin.
  - (d) Zone of calcification: The matrix becomes calcified and chondrocytes degenerate, leaving empty lacunar spaces.
  - (e) Zone of ossification: Empty lacunar spaces are invaded by osteoprogenitor cells and blood vessels. Osteoprogenitor cells differentiate into osteoblasts, which lay down bone on the surface of the calcified cartilage matrix.





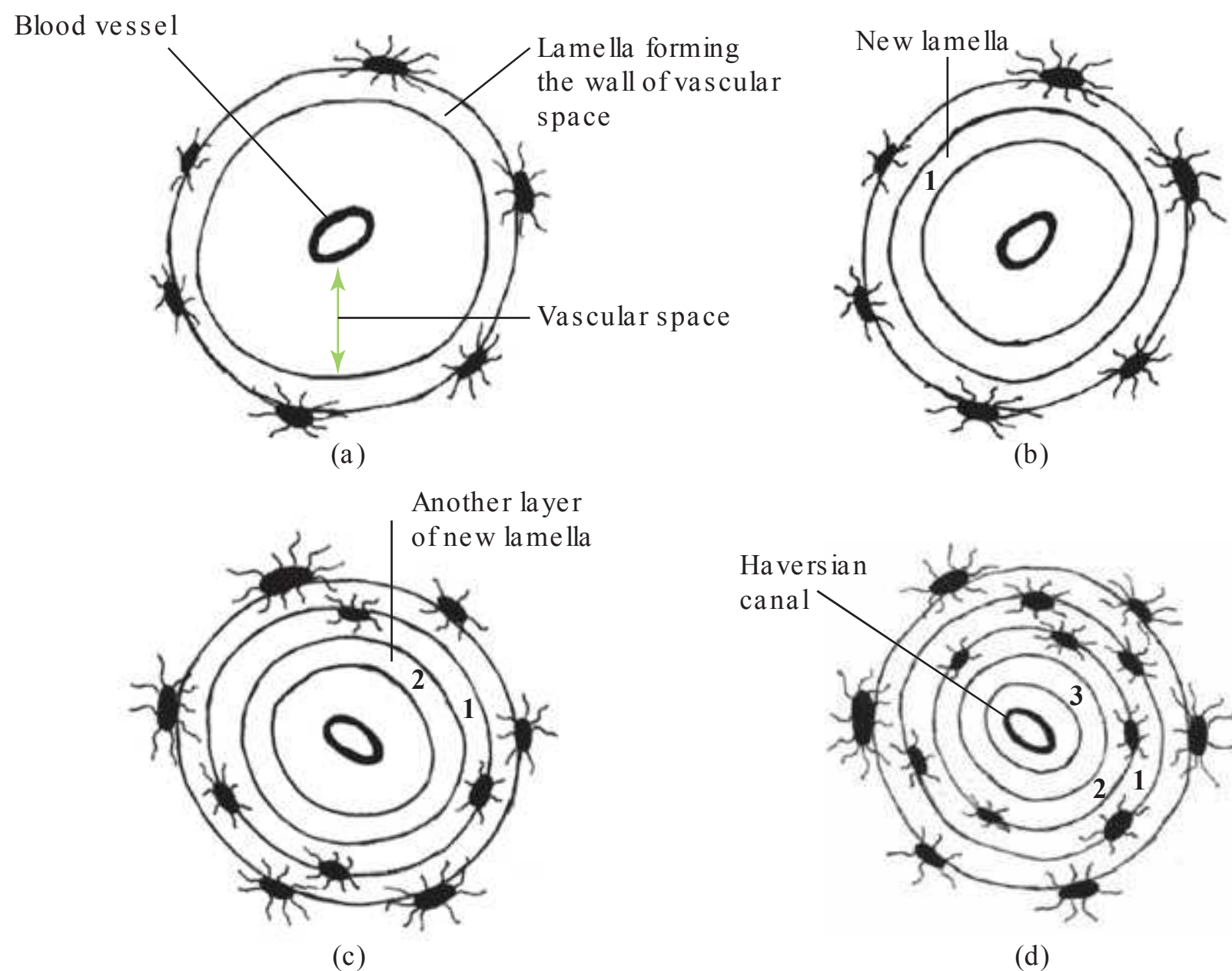
**Figure 7.14** Section of developing long bone showing endochondral ossification.

### **REMODELLING—THE FORMATION OF SECONDARY BONE**

- The bone formed by both intramembranous and endochondral ossification is woven (or primary) bone.
- In adults, the woven bone of both compact and spongy bones is replaced by the lamellar (secondary) bone.
- Components of the woven bone are irregularly arranged.
- Large vascular spaces enclosed by the woven bone (Fig. 7.15a) are lined by osteoprogenitor cells. These osteoprogenitor cells differentiate into osteoblasts.
- Osteoblasts lay down concentric layers of bone on the surface of the vascular space. This results in narrowing of the vascular space and gives rise to primary osteon (Fig. 7.15).
- Primary osteons are further remodelled by osteoclasts and osteoblasts and get replaced by secondary osteons or Haversian systems.



- When the new osteon is completed, the remnants of the previous osteon are called interstitial osteons; they are present between the adjacent Haversian systems.
- In an osteon, the oldest lamella is farthest from blood vessels (Fig. 7.15d).
- Formation of secondary osteons continues throughout life.



**Figure 7.15** Formation of Haversian system. (a) In the woven bone, the blood vessel is present in a large vascular space which is surrounded by the bone. (b–d) New lamellae are formed on the wall of vascular space. With each new lamella formed, the vascular space narrows. Finally, the narrow vascular space becomes the Haversian canal (d). Note that the most recent lamella [lamella number ‘3’ in (d)] forms the wall of the Haversian canal.

The events taking place during intramembranous and endochondral ossification have been summarised in Table 7.1.

**Table 7.1** Summary of Events Taking Place During Intramembranous and Endochondral Ossification

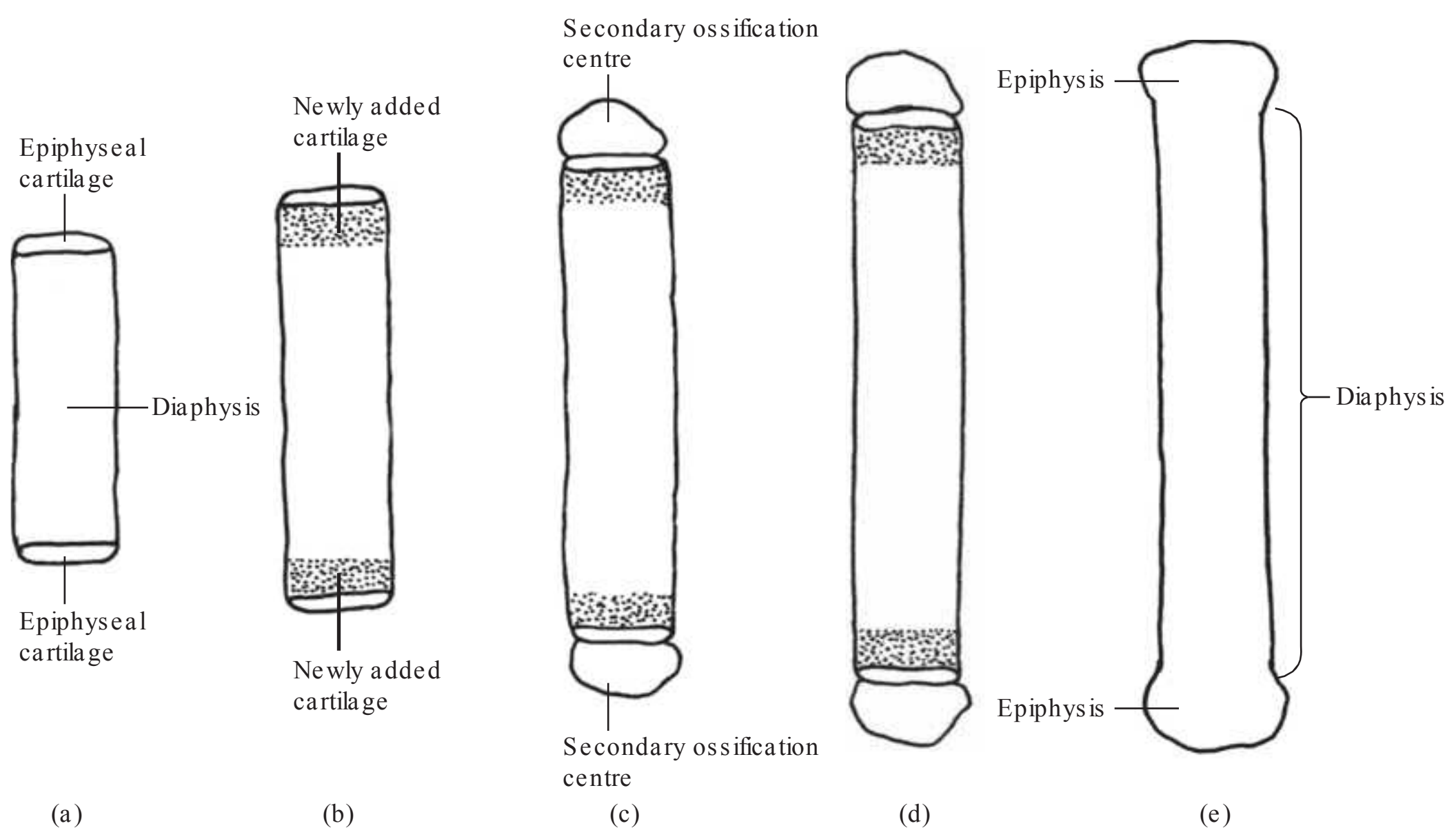
Intramembranous ossification	Endochondral ossification
<ul style="list-style-type: none"> <li>• It gives rise to flat bones of skull</li> <li>• Mesenchymal cells (Fig. 7.11a and b) differentiate into osteoprogenitor cells, and these cells give rise to osteoblasts. The ossification centre is formed</li> <li>• Several centres of ossification throughout the mesenchymal tissue are formed (Fig. 7.11d). As more new bone is added by these centres, these centres eventually fuse with each other. The fusion of ossification centres results in the formation of scattered, irregular trabeculae</li> <li>• Fusion of trabeculae gives rise to spongy bones (Figs 7.11e and 7.12)</li> <li>• The new bone is added on the surface of trabeculae. The space between the adjacent trabeculae reduces and eventually disappears and the spongy bone is converted into the compact bone</li> </ul>	<ul style="list-style-type: none"> <li>• It begins in the hyaline cartilage and gives rise to long bones</li> <li>• It involves the following steps: <ul style="list-style-type: none"> <li>(a) Formation of primary areolae (Fig. 7.13a–c)</li> <li>(b) Formation of periosteal collar (Fig. 7.13c)</li> <li>(c) Formation of primary and secondary centres of ossification (Fig. 7.13d–f)</li> <li>(d) Growth of the bone: The primary and secondary centres of ossification do not fuse till adulthood. The cells in the epiphyseal cartilage proliferate and add a new cartilage at the metaphyseal ends of the diaphysis; later the newly formed cartilage gets ossified</li> <li>(e) Remodelling—the formation of the secondary bone (Fig. 7.15)</li> </ul> </li> </ul>

## BONE GROWTH

During bone growth, new bone is laid down over the pre-existing bone. Simultaneously, resorption of the pre-existing bone also takes place, and this process helps in maintaining the shape of the bone. Naturally, if the bone has to grow, the rate of bone formation has to be greater than the rate of its resorption.

### GROWTH OF THE LONG BONE

- The longitudinal growth of the bone depends on the interstitial growth of epiphyseal cartilage. In this manner, the length of the shaft increases at both ends, and each end of the bone moves progressively apart (Fig. 7.16).
- The longitudinal growth of the bone continues till an individual attains puberty. The hormonal changes at puberty cause the transformation of epiphyseal cartilage into bone, and this results in fusion of epiphysis with diaphysis.
- Width of the bone is increased by deposition of bones at the outer surface by the osteoprogenitor cells in periosteum (appositional growth).
- Osteoclasts remove the bone from the endosteal surface and increase the size of the medullary cavity. Thus, the diameter of the bone increases, but the thickness of its wall does not alter much.

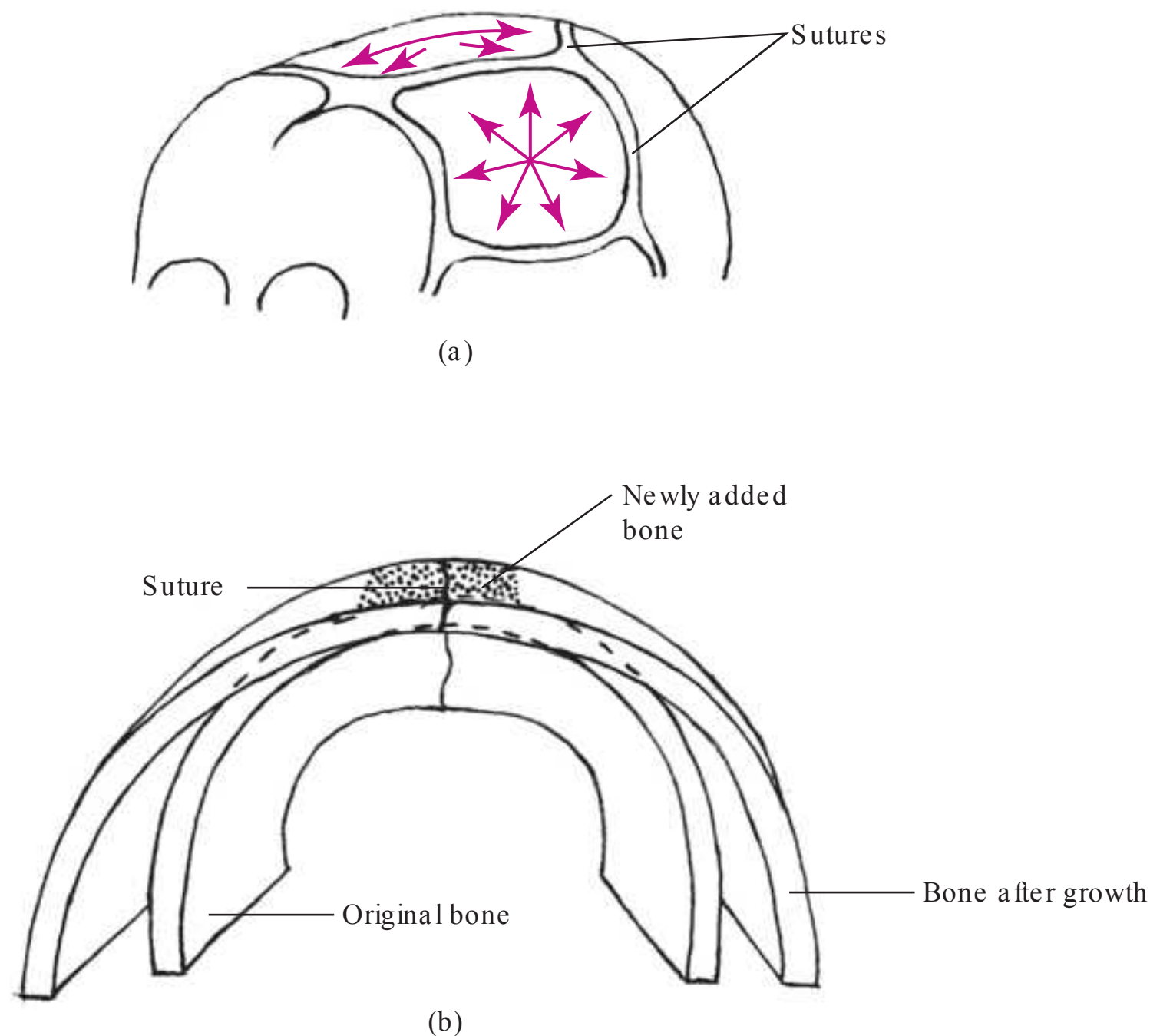


**Figure 7.16** Diagram showing growth of long bone. The cells in the epiphyseal cartilage proliferate, and new cartilage is added at the metaphyseal ends of the diaphysis of the growing bone (a and b). As the new cartilage is added at both ends of diaphysis, the growing bone increases in length, and as a result, the two epiphyseal plates move apart (c and d). Finally, the epiphyseal plate is transformed into bone and epiphysis fuses with diaphysis (e).

### GROWTH OF THE FLAT BONE

- In between the adjacent flat bones of the skull lies a thin layer of connective tissue called sutures.
- The flat bones increase in size by appositional growth.
- The new bone is added at the sutures and on the convex surface of the bones. At the same time, there is resorption of bones from the inner surface (Fig. 7.17).
- As the bones grow, their shape also changes, and they become less curved. All these changes help in increasing the size of the cranial cavity (Fig. 7.17).





**Figure 7.17** Diagram showing the growth of fat bone. (a) The arrows indicate the directions in which the bone grows. (b) The bone after growth—both increase in the size and change in the shape contribute to increase in the size of the cranial cavity.

### **BONE GROWTH SUBSEQUENT TO FRACTURE**

- Fracture is accompanied by haemorrhage due to the rupture of blood vessels of the bone, and a haematoma (clotted blood in a tissue or organ, caused by a rupture in a blood vessel) is formed.
- Macrophages remove the dead and damaged cells. The osteoprogenitor cells of periosteum and endosteum proliferate and differentiate into fibroblasts, which form the connective tissue that fills the gap between the fractured ends of the bone. The cells of the connective tissue differentiate into chondrocytes which form hyaline cartilage. All these events help in formation of new tissue which fills the gap at the fracture site; this tissue is known as callus.
- Endochondral ossification of the callus causes formation of woven bone.
- Subsequently, the woven bone is remodelled into lamellar bone.

### **FACTORS AFFECTING BONE GROWTH**

Bone development is influenced by a number of factors, including nutrition, hormonal secretions and physical exercise.

#### **Nutritional Factors**

- Vitamin C: Vitamin C is required in collagen synthesis; its deficiency (scurvy) causes poor bone growth and delays the healing process after the fracture of the bone.
- Vitamin D: Vitamin D is necessary for the proper absorption of calcium in the small intestine. In the absence of this vitamin, calcium is poorly absorbed; as a result, the bone matrix is deficient in calcium

and the bones are likely to be deformed or very weak. This condition is called rickets in children and osteomalacia in adults.

- Vitamin A: Both deficiency and excess of vitamin A cause short stature. Its hyposecretion slows the bone growth, whereas in hypersecretion the ossification is accelerated, causing early fusion of epiphysis.

## Hormones

Hormones that affect bone growth and development include growth hormone, parathyroid hormone, calcitonin and sex hormones.

- Growth hormone: It is also known as somatotropin. It is secreted by the pituitary gland. It plays an important role in the growth of the body. In the bone, it stimulates growth of epiphyseal plates.
- Parathyroid hormone: It is secreted by the parathyroid gland. It is released in response to low calcium levels in the blood. It stimulates osteoclasts to break down bone tissue, and as a result, calcium salts are released into the blood.
- Calcitonin: It is secreted by the parafollicular cells of the thyroid gland. It is released in response to high calcium levels in the blood. It inhibits osteoclast activity, allowing osteoblasts to form bone tissue. As a result, the excessive calcium is stored in the bone matrix.
- Sex hormones: Their deficiency delays puberty; hence, the fusion of epiphysis occurs late and this results in tall stature. Conversely, the hypersecretion of sex hormones causes the fusion of epiphysis earlier and this results in short stature.

## Physical Exercise

The stresses of physical activity result in growth and strengthening of bone tissue.

## BLOOD SUPPLY OF A LONG BONE

The long bone is supplied by four sets of arteries: the principal nutrient, the metaphyseal, the epiphyseal and the periosteal arteries.

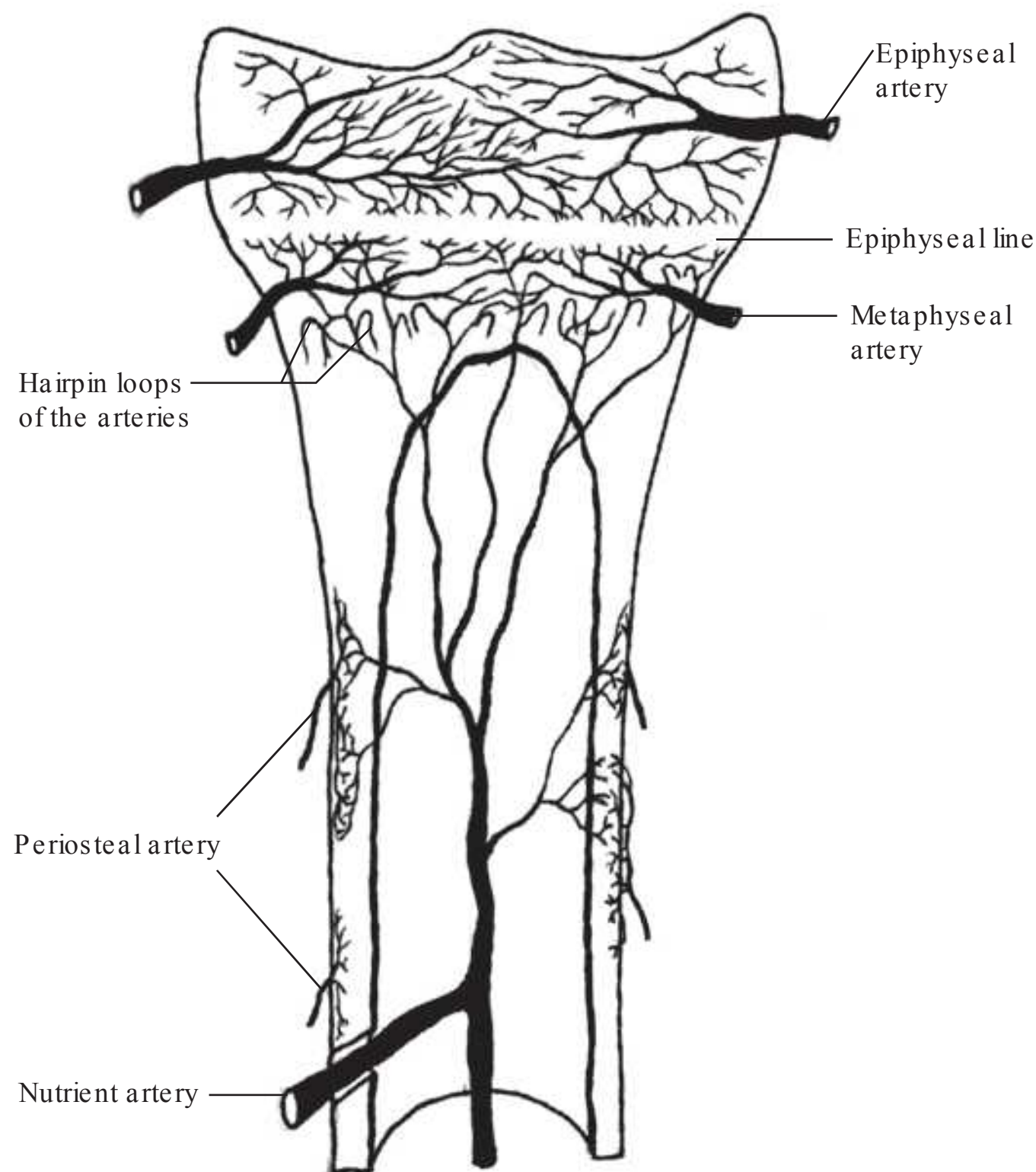
### BLOOD SUPPLY TO THE SHAFT (Fig. 7.18)

Diaphysis is supplied by the principal nutrient artery and periosteal arteries.

#### 1. The principal nutrient artery

- The principal nutrient artery enters the middle of diaphysis through nutrient foramen, and it traverses the full thickness of the cortex through a canal to enter the marrow cavity.
- The nutrient foramina and canal are directed obliquely away from the growing end of the bone. The growing end of the bone is the end which grows for the longer period; this is because at this end the fusion of the epiphysis with the diaphysis occurs later than the opposite end.
- The nutrient artery supplies the inner two-thirds of the cortex, medullary cavity and metaphysis. The branches of the nutrient artery pass through the Volkmann's canal and supply the Haversian systems.
- At the metaphysis, branches of the nutrient artery anastomose with the epiphyseal and metaphyseal arteries.





**Figure 7.18** Blood supply of a long bone.

## 2. Periosteal arteries

- These arteries are numerous, and they are located beneath the muscular and ligamentous attachments.
- They ramify beneath the periosteum; some branches enter the Volkmann's canals and supply the outer one-third of the bone.

## BLOOD SUPPLY TO THE ENDS OF THE BONE

- The arteries supplying the ends of a long bone arise from the arteries that supply the joint. The ends of a long bone are supplied by numerous metaphyseal and epiphyseal arteries.
- In growing bones, these arteries are separated by the epiphyseal cartilaginous plates. After maturity, these arteries anastomose with each other.

## BLOOD VESSELS AT THE METAPHYSIS

- The arrangements of the blood vessels at the metaphysis make the blood circulation sluggish. Here, the branches of the nutrient artery show hairpin-like loops and continue with the vein.
- The metaphysis is a highly vascular region of the bone and also the circulation of blood is sluggish here; both these factors help bacteria to settle in this region of the bone and cause osteomyelitis (infection of the bone).

CLINICAL CORRELATES

Osteopetrosis

- Osteopetrosis is a genetic disorder. It occurs due to defect in osteoclast function; as a result, bones become brittle.

Osteoporosis

- Osteoporosis is a condition characterised by reduction in bone density and hence the bone is prone to fracture. Senile and postmenopausal osteoporoses are the most common forms.

Bone Tumours

- Osteoid osteoma and osteoblastoma are benign tumours; osteosarcoma is a malignant tumour.

KEYPOINTS

Bone Cells

Bone cells	Location and organisation	Function
Osteoblasts	They form a single-cell thick layer on the surface where new bone is being formed (Figs 7.11c and d, and 7.12)	These are bone-forming cells, and they synthesise organic components of the bone matrix
Osteocytes	They lie in lacunae. Lacunae are connected with each other by canaliculi, and within these canaliculi there are fine cytoplasmic extensions of osteocytes by which the adjacent osteocytes are in contact with each other (Figs 7.1, 7.2 and 7.9; PMG 7.2)	Maintenance of the bone matrix
Osteoclasts	Multinucleated cells are located in Howship’s lacuna (Figs 7.3 and 7.12)	Bone resorption

Coverings of the Bone

	Periosteum	Endosteum
Location	External surface of the bone	Inner surface of the bone
Organisation	Two layers: the outer fibrous layer and the inner osteogenic layer (Figs 7.2 and 7.9)	Single layer of osteoprogenitor cells (Fig. 7.2)
Function	Bone growth and repair	Same as periosteum

Types of Bone Based on Their Histological Appearance

Woven bone	Lamellar bone
<ul style="list-style-type: none"><li>• It has irregularly arranged collagens and osteocytes</li><li>• It is replaced in adults by the lamellar bone</li></ul>	<ul style="list-style-type: none"><li>• It is made up of concentric bony layers or lamellae</li><li>• It is of two types—compact and spongy bones</li></ul>



Lamellar Bone

Compact (Fig. 7.9; PMG 7.1 and 7.2)	Spongy (Fig. 7.10)
<ul style="list-style-type: none"><li>• The unit of the compact bone is Haversian system. It consists of a central canal and surrounding lamellae and osteocytes</li><li>• Based on their location within the bone, lamellae can be classified as inner circumferential lamellae, outer circumferential lamellae and interstitial lamellae</li></ul>	<ul style="list-style-type: none"><li>• It consists of a network of trabeculae separated by interconnecting spaces, resembling a sponge</li><li>• The space around the trabeculae contains the bone marrow</li></ul>

SELF-ASSESSMENT

1. Mention the types of bone cells, their location and functions.
2. What are the components of bone matrix?
3. Compare the periosteum and endosteum.
4. Describe an osteon.
5. Describe the parts of a long bone and its blood supply.
6. Where are spongy and compact bones found in the body?
7. Describe the intramembranous and endochondral ossification.

# Nervous Tissue

- Nervous tissue is one of the four basic types of tissues in the human body and it is conferred with special properties of excitability and conductivity.
- Nerve cells respond to the changes in internal or external environment (excitability) and generate nerve impulse which is conducted by nerve fibres (conductivity).
- The nervous tissue consists of two types of cells: neurons, which transmit impulses, and glial cells, which are supporting cells.

## NEURONS

- Neuron is the structural and functional unit of the nervous system.
- Neurons can differ in size and shape; however, most of the neurons have the same parts as described in the following section.

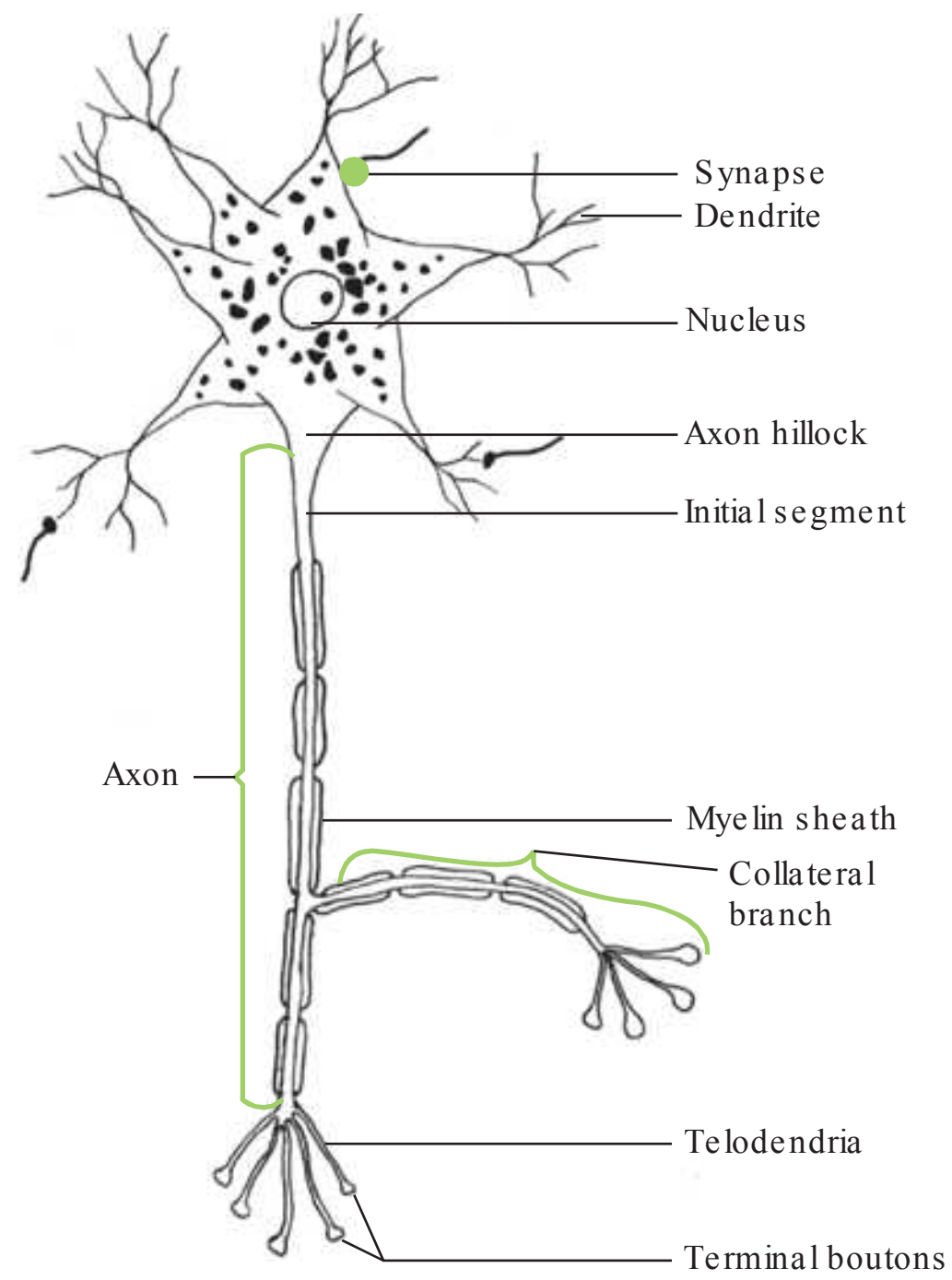
### PARTS OF NEURON

Each neuron consists of a large cell body (with its processes) and a single axon (Fig. 8.1). The processes of the cell body are called dendrites.

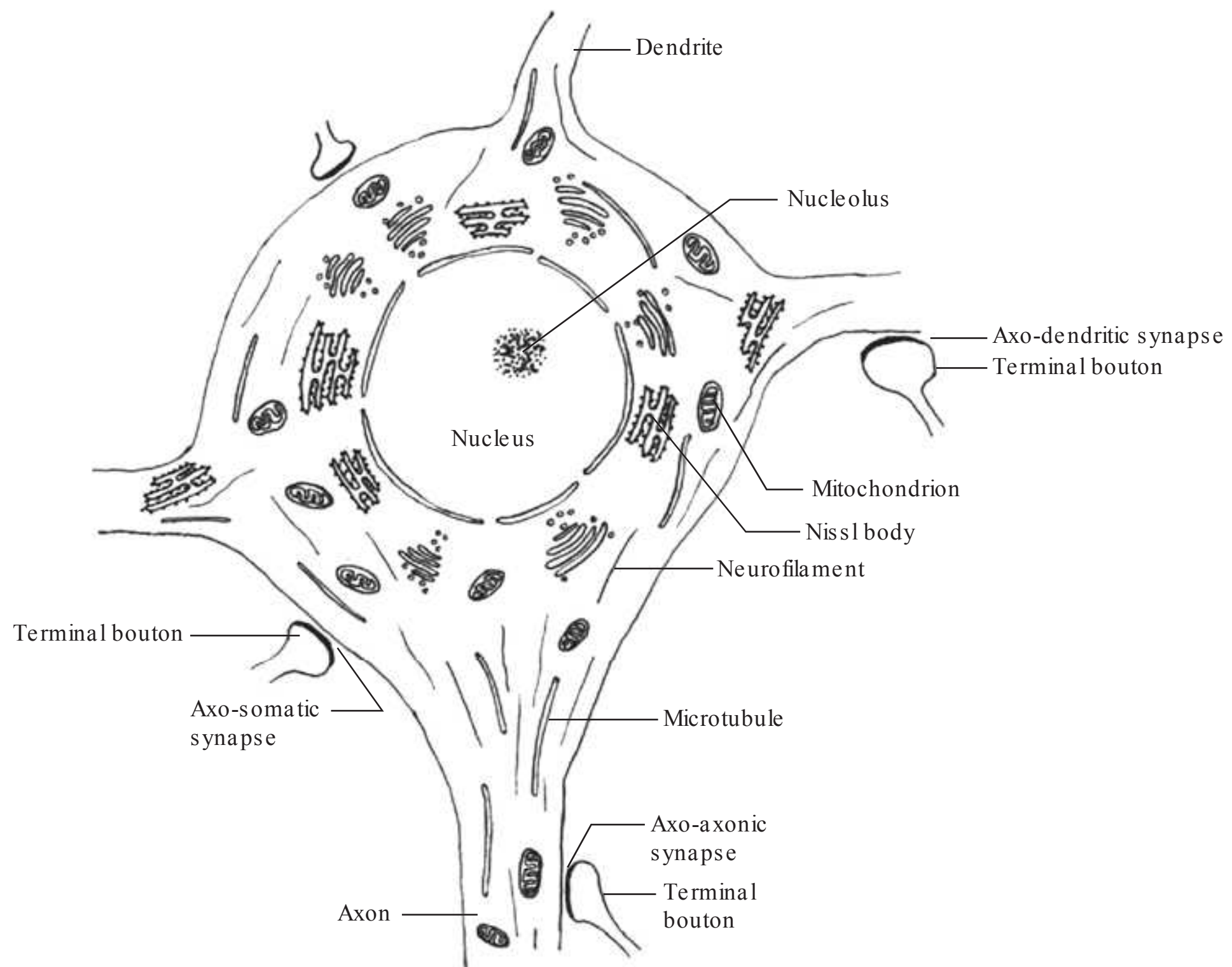
#### Cell Body

- The cell body is also called perikaryon.
- It contains a large, round, centrally placed nucleus. The nucleus is surrounded by cytoplasm containing various cell organelles and inclusions.
- The cytoplasm contains the following:
  - (a) Clumps of rough endoplasmic reticulum called Nissl bodies (Fig. 8.2): They stain with basic dyes. They are more in number in motor cells than in sensory cells and help in the synthesis of new proteins. Nissl bodies are also present in dendrites but never in an axon.
  - (b) Well-developed Golgi complexes: These are present near the nucleus (Fig. 8.2).
  - (c) Large number of mitochondria and lysosomes: These are distributed all over the cytoplasm.
  - (d) Lipofuscin granules: These are residual bodies formed by lysosomal activity.
  - (e) Neurofilaments and microtubules: These form the cytoskeleton and are present throughout the cytoplasm (Fig. 8.2). Neurofilaments are the intermediate filaments of nerve cells; they form an anastomosing network surrounding the nucleus. The cytoskeleton also extends into the dendrites and axon.
- An extension of the cell body which connects the cell body with the axon is called axon hillock (Fig. 8.1). In this region, Nissl bodies are absent.





**Figure 8.1** Parts of neuron.



**Figure 8.2** Ultrastructure of cell body of a neuron.

## Axon

- Axons are also called nerve fibres.
- Each neuron has a single axon. Some axons may further give collateral branches.
- The axon conducts nerve impulse away from the cell body to the axonal terminal.
- It begins from the axon hillock and ends at the terminal portion. The part of the axon between the axon hillock and the point at which myelin sheath begins is called initial segment (Fig. 8.1). At the terminal end, the axon divides into numerous branches called telodendria, which show swellings called terminal boutons at their ends (Fig. 8.1).
- Axon is covered by plasma membrane called axolemma and its cytoplasm is called axoplasm. It lacks Nissl bodies and Golgi complex (Fig. 8.2).

## Axonal Transport

- Various substances (such as newly synthesised proteins or worn-out cell organelles) are transported through the axons.
- When a substance is transported from the cell body to the axon terminals it is referred to as anterograde transport, whereas the transport in opposite direction, that is from axon terminal to the cell body, is referred to as retrograde transport.

## Dendrite

- Most neurons have multiple dendrites.
- Dendrites are cytoplasmic extensions of the cell body (Fig. 8.1). These structures are highly branched, and this branching helps to increase the surface area.
- These structures are specialised for receiving signals from sensory receptors or from neighbouring nerve cells through synapses.
- These are unmyelinated; their cytoplasm is devoid of Golgi complex.
- Some dendrites have numerous small protrusions; these are called dendritic spines.

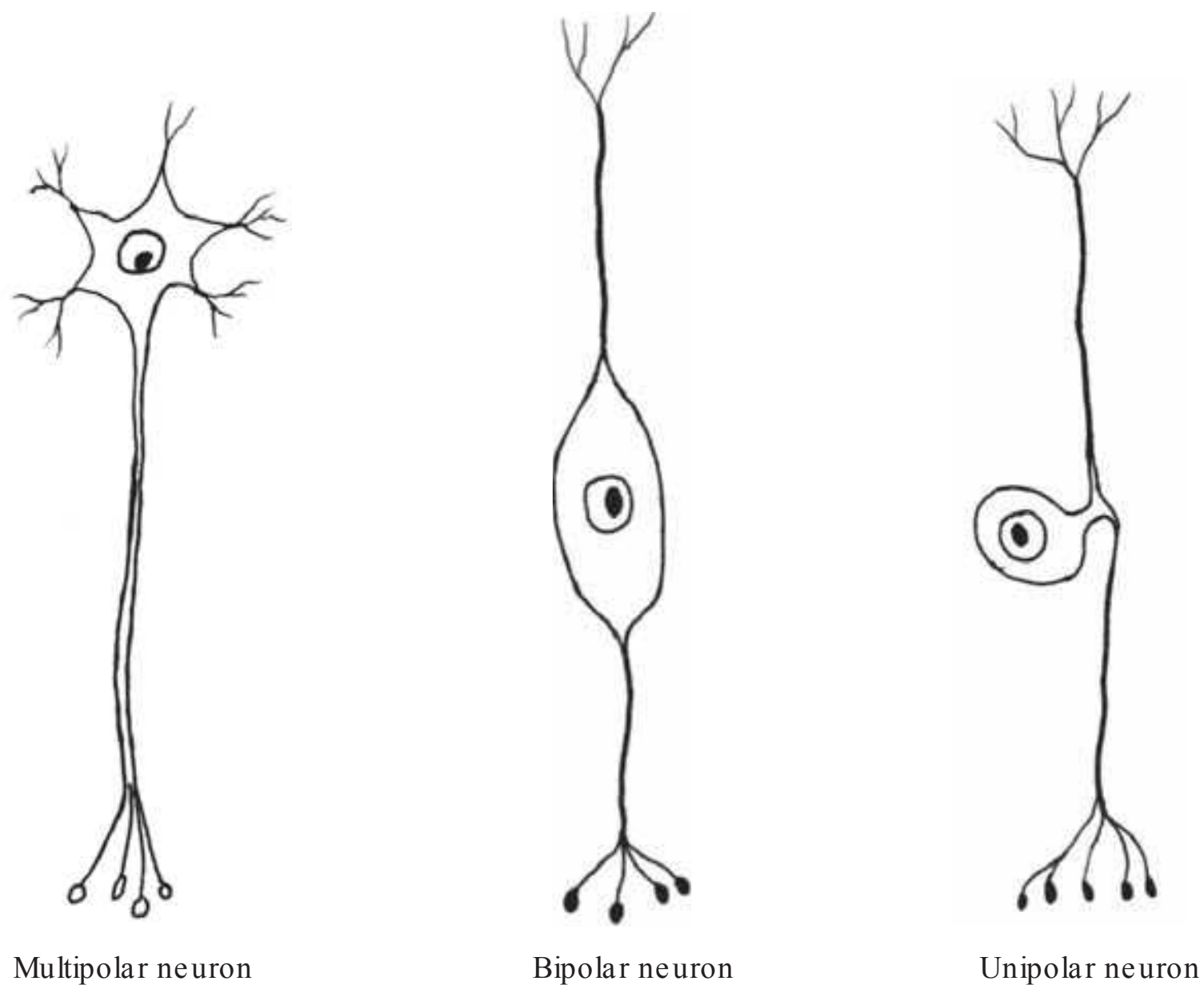
## TYPES OF NEURONS

Neurons can be classified on the basis of the arrangement of cell body processes and the functions they perform. They can also be classified on the basis of the length of axons.

### 1. On the basis of the arrangement of cell body processes, neurons are of three types (Fig. 8.3):

- Multipolar neuron
  - It is the most common type of neuron; it has two or more dendrites.
  - Example: Motor neurons.
- Bipolar neuron
  - It has one dendrite which arises from the pole of the cell body opposite to the pole at which the axon begins.
  - Examples: Neurons in vestibular and spiral ganglia (of vestibulocochlear nerve), in retina and in olfactory cells of nasal mucosa.
- Unipolar neurons
  - The cell body has a common process which bifurcates into an axon and a single dendrite.
  - Developmentally, they are derived from bipolar neurons; hence they are also known as pseudounipolar neurons.
  - Example: Neurons in dorsal root ganglia.





**Figure 8.3** Types of neurons.

2. **On the basis of the functions**, neurons are of two types—sensory and motor (see Figure 8.9 for organisation of sensory and motor neurons).
  - Sensory neuron
 

These carry impulses from the sensory receptor to the central nervous system (CNS). These are pseudounipolar neurons.
  - Motor neuron
 

These carry impulses from the CNS to the effector cells. These are multipolar neurons.
3. **On the basis of the length of axons**, neurons are classified into two types—Golgi type I and type II.
  - Golgi type I
    - These neurons have long axons and form the tracts in the CNS.
    - Example: Pyramidal cells of motor cortex in cerebrum.
  - Golgi type II
    - These neurons have short axons.
    - Example: Interneurons.

## GLIAL CELLS

- These are all non-neural, supporting cells of the CNS. They have the capacity to divide. However, they are not involved in conduction of nerve impulse.
- There are four types of neuroglial cells: oligodendrocytes, astrocytes, microglia and ependymal cells.

### OLIGODENDROGLIA (see Fig. 8.7)

- These cells are responsible for myelination of axons in the CNS. They are present both in grey and white matter.

- These cells have spherical nuclei and several short cell processes.
- A single cell is responsible for myelination of segments of several neurons.

### **ASTROCYTES (Fig. 8.4)**

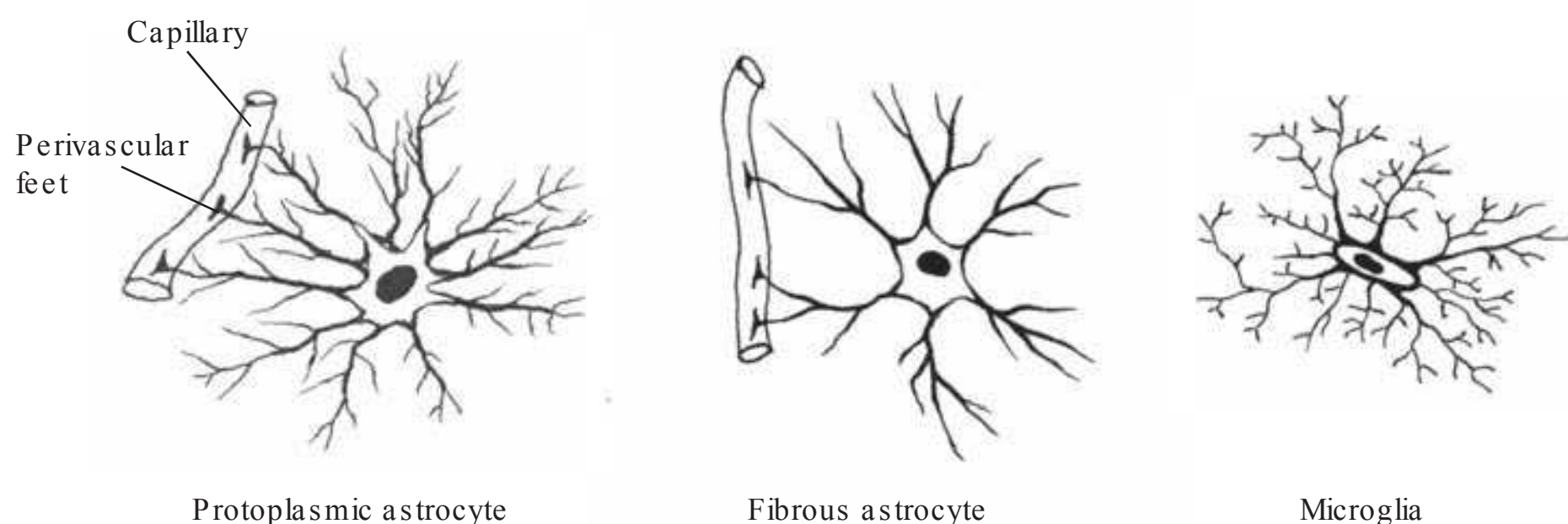
- They provide structural support to nervous tissue and participate in blood–brain barrier.
- They have large nuclei and long branching cytoplasmic processes in all directions.
- The ends of the cytoplasmic processes expand and surround the capillaries; these expanded ends are called perivascular *feet*.
- Astrocytes are of two types: protoplasmic and fibrous astrocytes.
- Protoplasmic astrocytes are present mostly in grey matter; they have highly branched cytoplasmic processes.
- Fibrous astrocytes are found mainly in white matter; their cytoplasmic processes are less branched than those of protoplasmic astrocytes.

### **MICROGLIA (Fig. 8.4)**

- Microglia are the smallest and least common of the glial cells; they are present in both grey and white matter.
- These cells perform phagocytic function at the site of injury.
- These cells are of mesodermal origin.

### **EPENDYMAL CELLS**

- These are columnar cells; they are arranged as simple epithelium that lines the ventricles of brain and central canal of the spinal cord.
- In some regions these cells are ciliated.
- These cells do not rest on basement membrane; they have processes at the base extending into the grey matter.



**Figure 8.4** Types of glial cells. (See Fig. 8.7 for oligodendrocyte.)

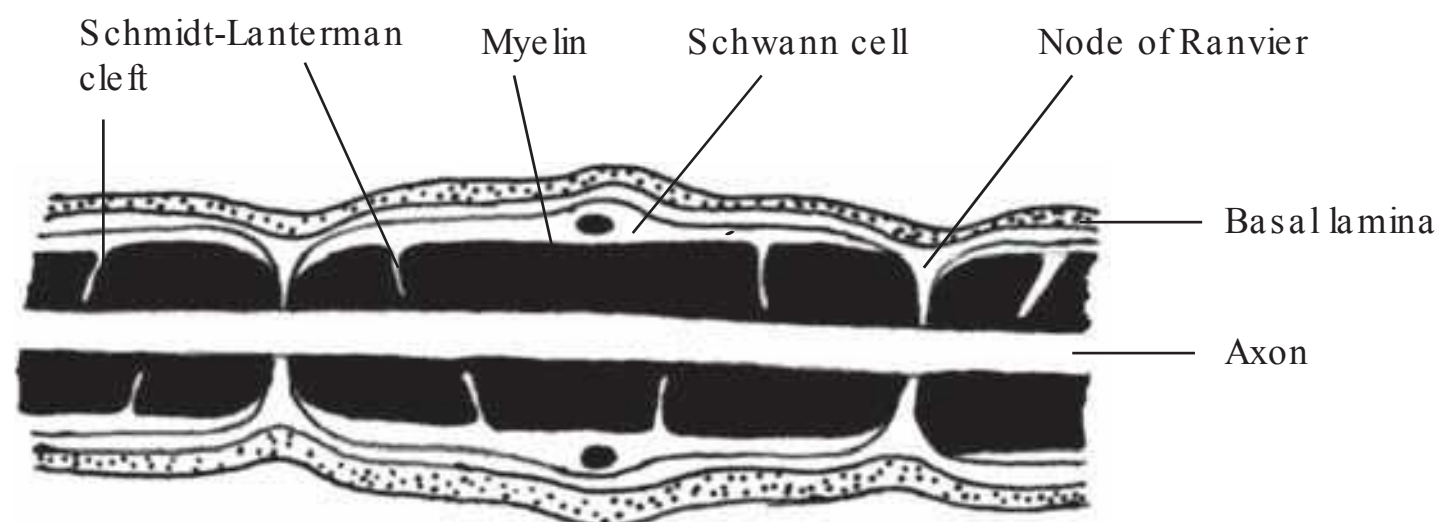


## TYPES OF NERVE FIBRES

These may be myelinated or non-myelinated.

### MYELINATED NERVE FIBRES (Fig. 8.5)

- In peripheral nervous system (PNS), Schwann cells provide structural support to all nerve fibres. Schwann cells form a sheath around the axon and form the outermost layer of a nerve fibre, called neurilemma, also known as sheath of Schwann or neurolemma. Schwann cell is surrounded by a basal lamina (or external lamina).
- In some fibres, Schwann cells additionally form myelin sheath; these fibres are called myelinated nerve fibres (Fig. 8.1). These nerve fibres in which myelin sheath is not formed, that is Schwann cells only provide structural support, are non-myelinated nerve fibres.
- Schwann cells deposit concentric layers of myelin around the axon to form myelin sheath. In myelinated fibres, one Schwann cell covers only a short segment of the axon. The small part of the axon present in between two adjacent Schwann cells (the part that is devoid of myelin sheath) is called node of Ranvier.
- Myelin is a mixture of lipoproteins and acts as an insulator. Since myelin acts as an insulator, impulses are generated only at the nodes of Ranvier and this helps in faster conduction of the impulses. This is called saltatory conduction.
- In CNS, myelin sheath is formed by oligodendrocytes.



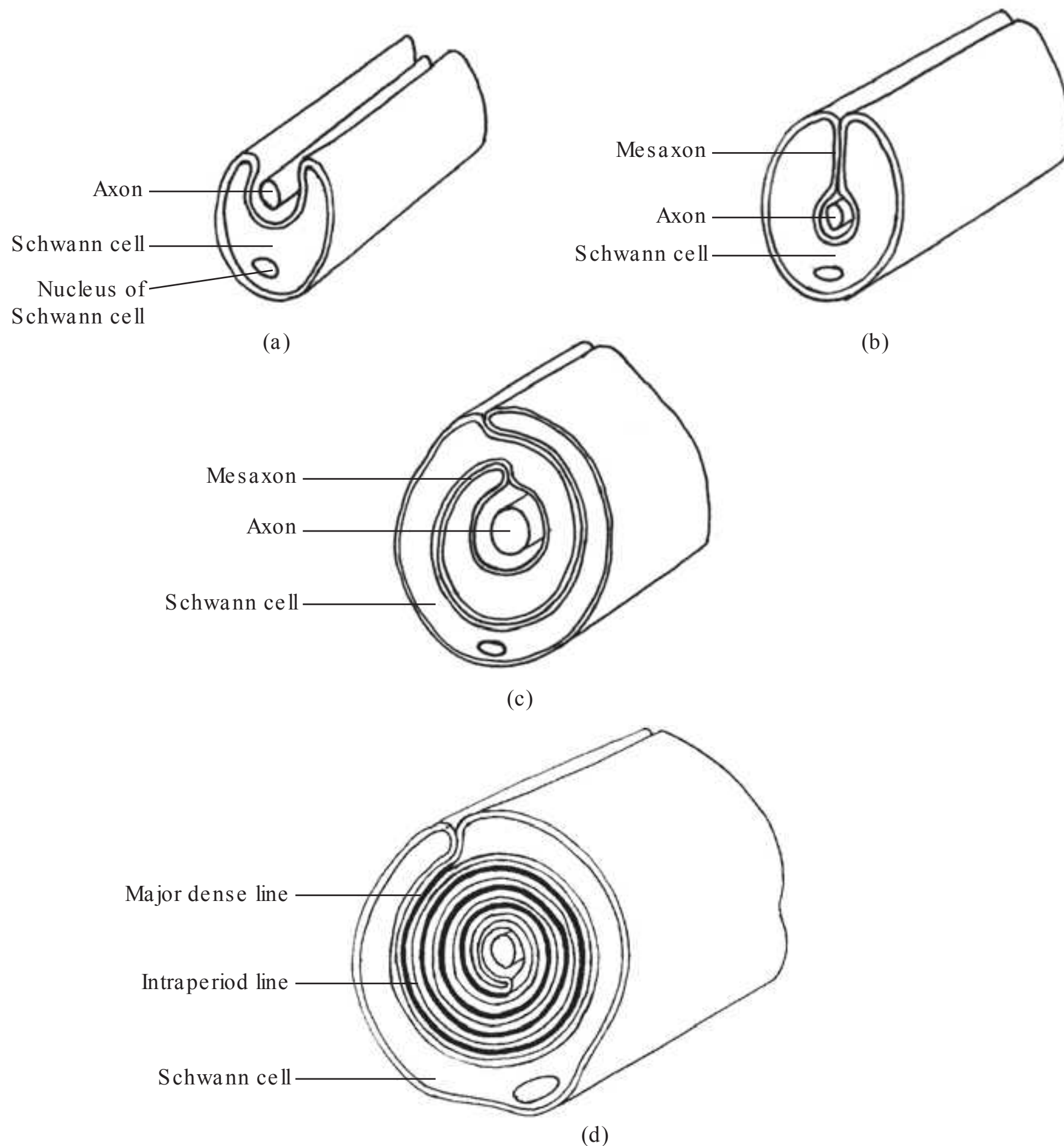
**Figure 8.5** Myelinated nerve fibre.

### Myelination

In PNS myelin is formed by Schwann cells, whereas in CNS it is formed by oligodendrocytes.

#### *In Peripheral Nervous System*

- First, the Schwann cell completely invests the axon (Fig. 8.6a); as a result, a double-layered fold called mesaxon is formed (Fig. 8.6b).
- Schwann cell rotates around the axon; as it rotates the mesaxon spirals around the axon, forming several layers of mesaxon concentrically arranged around the axon (Fig. 8.6c), just like rolling up a calendar.
- During this process, the cytoplasm of the Schwann cell is pushed to the periphery along with the nucleus (Fig. 8.6d).
- Several layers of mesaxon concentrically arranged around the axon are referred to as myelin sheath (Fig. 8.6d). The myelin sheath consists of alternating light and dark layers. Light layers are called intraperiod lines and are formed by the fusion of two outer layers of plasma membrane (Fig. 8.6d).



**Figure 8.6** Steps of myelination in peripheral nervous system.

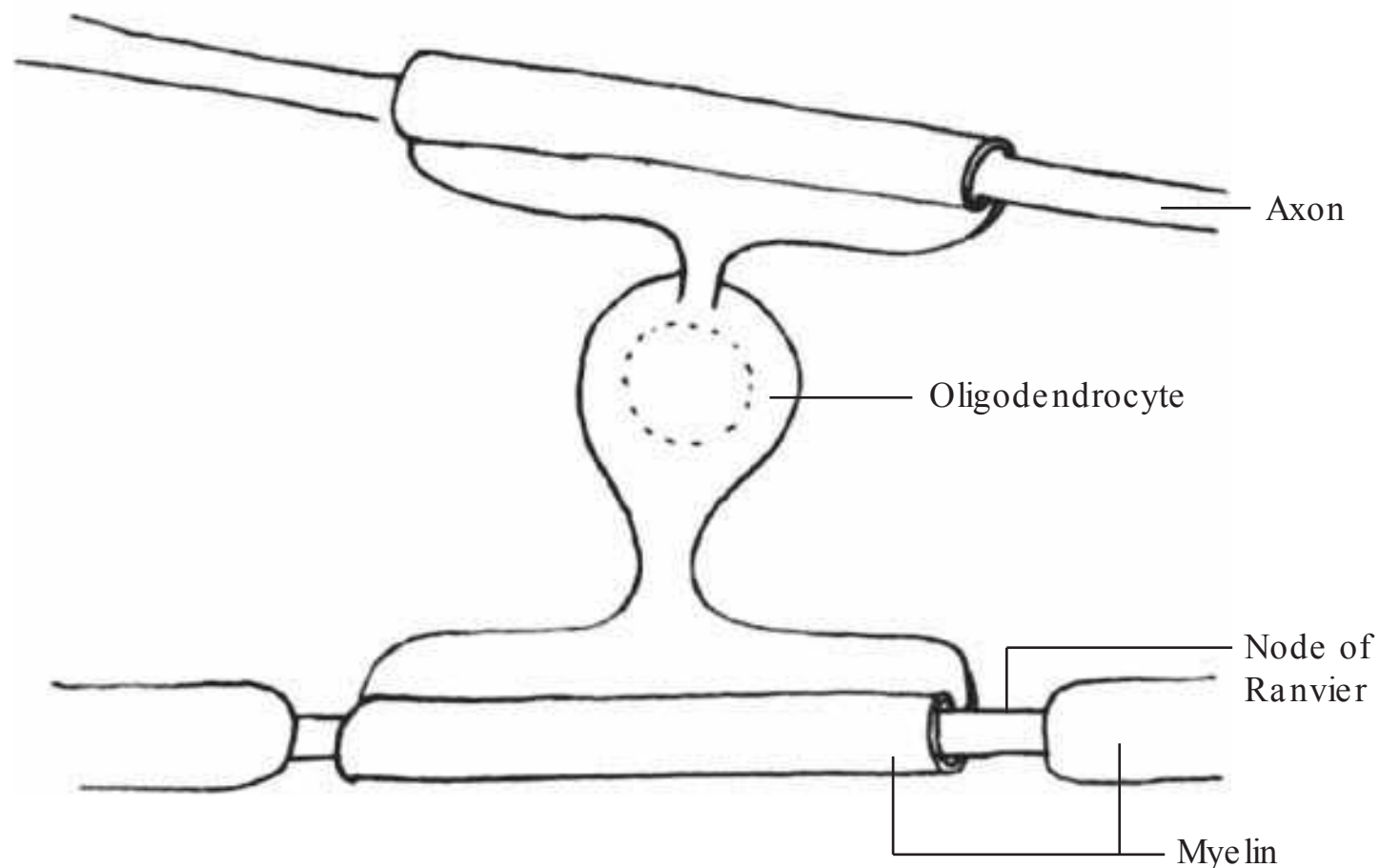
Dark layers are formed by fusion of two inner (cytoplasmic) layers of plasma membrane and are called major dense lines (Fig. 8.6d).

- As described earlier, when the mesaxon spirals around the axon, the cytoplasm of the Schwann cell is pushed to the periphery; however, some amount of cytoplasm remains in the myelin sheath at a few sites. The inner collar of cytoplasm surrounds the axon on the inner aspect of the myelin sheath while the outer collar of cytoplasm surrounds the myelin sheath (Fig. 8.6d). The inner and outer collars of cytoplasm of Schwann cells are continuous with each other at two locations—within the myelin sheath at Schmidt-Lanterman clefts (Fig. 8.5) and in the node of Ranvier at the perinodal cytoplasm.
- In PNS, several Schwann cells are involved in myelination of a single axon.

### *In Central Nervous System*

- Like Schwann cell, oligodendrocyte also wraps around the axon and forms myelin sheath (Fig. 8.7).
- Nodes of Ranvier are present at regular intervals.
- Unlike in PNS, in CNS one oligodendrocyte deposits myelin around several axons through its processes.





**Figure 8.7** Myelination process in central nervous system.

### UNMYELINATED NERVE FIBRES

- In PNS, Schwann cells provide structural support to non-myelinated nerve fibres. Several nerve fibres invaginate the cytoplasm of Schwann cell without any spiralling of the mesaxon (see Fig. 8.9).
- In CNS, unmyelinated nerve fibres do not have any sheath around them; they run among the other cells.

## MEMBRANE POTENTIAL AND IMPULSE CONDUCTION

At rest (i.e. when nerve is not stimulated), the plasma membrane of a neuron is polarised, that is there is unequal distribution of ions inside and outside the neuron. This potential difference is known as resting membrane potential and its value is  $-70$  mV.

### ACTION POTENTIAL

When the nerve is stimulated, the permeability of the plasma membrane to various ions present inside and outside the neuron changes, and this results in action potential or nerve impulse.

### IMPULSE CONDUCTION

- The action potential generated due to stimulus spreads to the entire nerve cell membrane in a non-myelinated neuron. The conduction of impulse can be orthodromic or antidromic. Usually, the impulse is conducted from dendrites to the axon terminal; this is orthodromic conduction. When the conduction of impulse is in the opposite direction it is known as antidromic conduction.
- At the synapse (described later), the conduction of impulse is unidirectional; the orthodromic impulse that reaches the axon terminal crosses the synapse and stimulates the dendrite of another neuron. The antidromic impulse that reaches the cell body and then the dendrites cannot cross the synapse.
- In myelinated nerve fibres, myelin acts as insulator; hence the impulse is generated only at the nodes of Ranvier, resulting in saltatory conduction.

## SYNAPSE

Synapses are contact points between neighbouring neurons for transmission of signals from one neuron to another.

### TYPES OF SYNAPSE

Synapses are classified on the basis of the part of the neuron taking part in the synapse and the method of nerve impulse transmission across the synapse.

**1. On the basis of the part of neurons taking part in synapse**, synapses can be of the following types (Fig. 8.2):

- Between axon and dendrite (axodendritic)
- Between axon and cell body (axosomatic)
- Between two axons (axoaxonic)
- Between two dendrites (dendrodendritic)

**2. On the basis of the method of nerve impulse transmission across the synapse**, synapses can be either chemical or electrical.

- Chemical synapse
- Electrical synapse

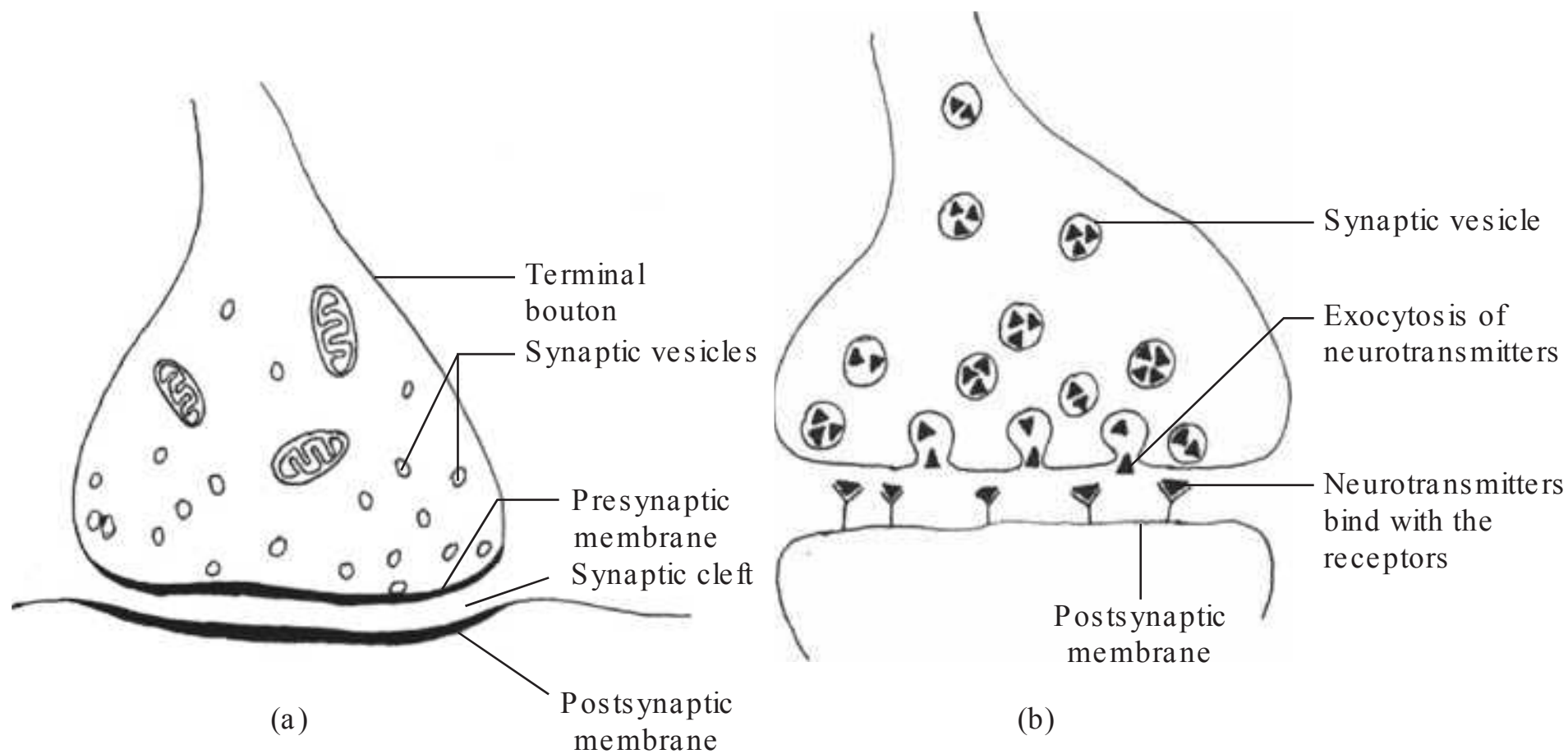
### Chemical Synapse

- A chemical (neurotransmitter) is released from the presynaptic neuron which acts on the postsynaptic neuron.
- The impulse travels in one direction.

#### *Components of Chemical Synapse*

- A synapse consists of three components, namely presynaptic and postsynaptic membranes and a synaptic cleft which separates the two (Fig. 8.8a).
- Presynaptic membrane: Terminal boutons of a presynaptic neuron coming in contact with the postsynaptic neuron form the presynaptic membrane. Terminal boutons contain numerous vesicles filled with chemical substances, the neurotransmitters. When the action potential reaches the terminal bouton, there is influx of calcium from the extracellular space; this causes release of neurotransmitters from the presynaptic membrane by exocytosis into the synaptic cleft (Fig. 8.8b).
- Synaptic cleft: Separating the pre- and postsynaptic membrane is a 20–30 nm wide space called the synaptic cleft (Fig. 8.8a). The neurotransmitter released from the presynaptic membrane diffuses across this space.
- Postsynaptic membrane: Postsynaptic membrane is the cell membrane of the second neuron taking part in synapse (Fig. 8.8a). In the region of synapse, the cell membrane is thick. The neurotransmitter binds with the receptors present on postsynaptic membrane (Fig. 8.8b). Based on the type of neurotransmitter, the effect on the postsynaptic membranes can be excitatory or inhibitory. For example, acetylcholine stimulates and  $\gamma$ -aminobutyric acid (GABA) inhibits the postsynaptic membrane.





**Figure 8.8** Synapse showing (a) the components of chemical synapse and (b) the release of neurotransmitters from the presynaptic neurons into the synaptic cleft and binding of neurotransmitters to the receptors on the postsynaptic membrane.

### Neurotransmitters

- These are produced by presynaptic neurons and cause either excitation or inhibition of the postsynaptic membrane.
- The most common neurotransmitters are acetylcholine and norepinephrine.

### Electrical Synapse

- In electrical synapse, ions pass from presynaptic neuron to postsynaptic neuron through gap junctions.
- The impulse can travel in both directions.
- Conduction of impulse is faster than through chemical synapse.

## CLASSIFICATION OF NERVOUS TISSUE

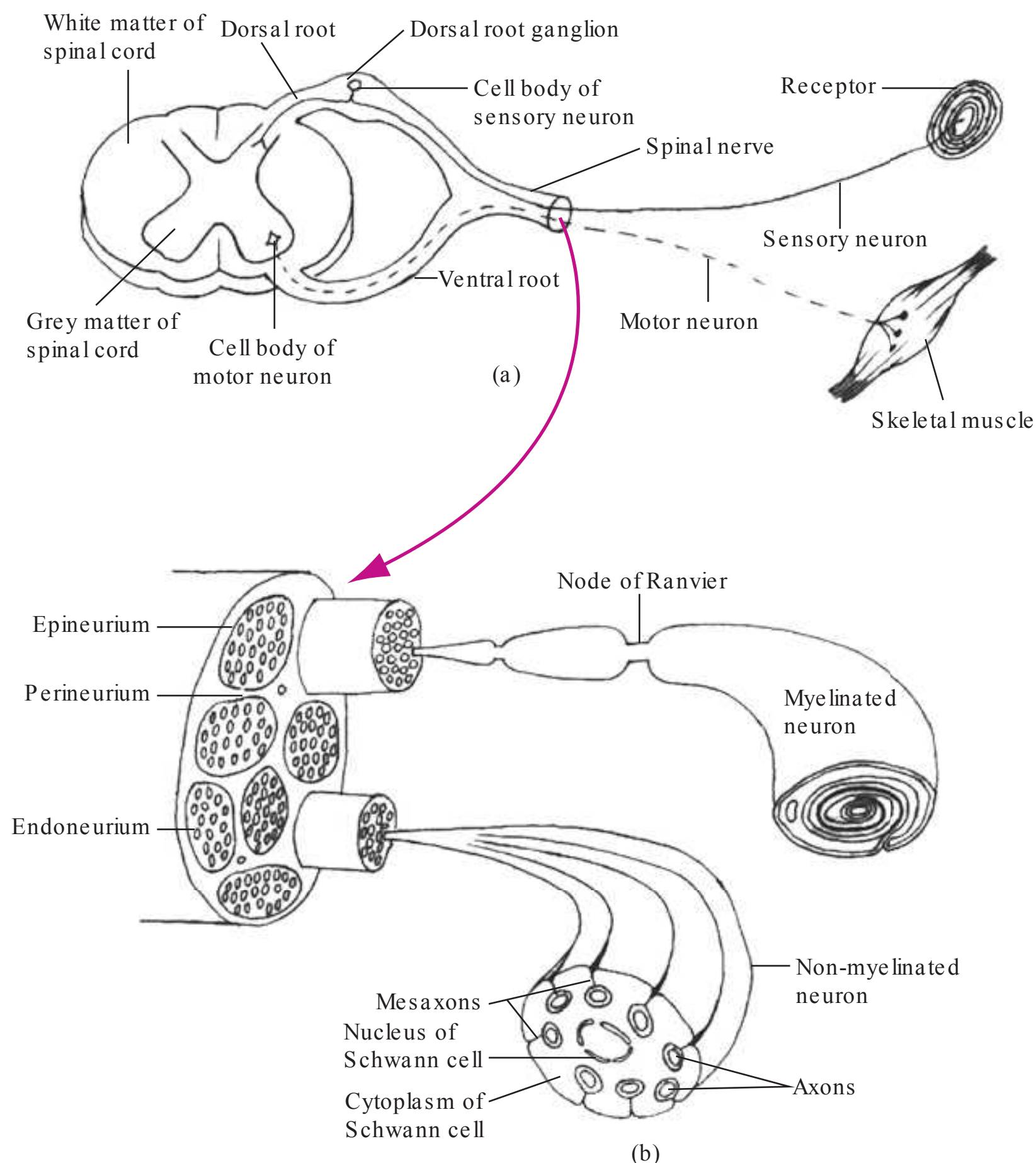
The entire nervous system has been classified anatomically and functionally.

- Anatomical classification: The entire nervous system is classified anatomically into central and peripheral nervous systems. The central nervous system includes brain and spinal cord (described in Chapter 21). The peripheral nervous system consists of 12 pairs of cranial nerves which arise from the brain, 31 pairs of spinal nerves which arise from the spinal cord and associated ganglia.
- Functional classification: Functionally, the nervous system is classified into autonomic and somatic nervous systems. The autonomic nervous system is concerned with control of involuntary organs (such as glands and heart). The somatic nervous system is concerned with control of voluntary movements.

## PERIPHERAL NERVES

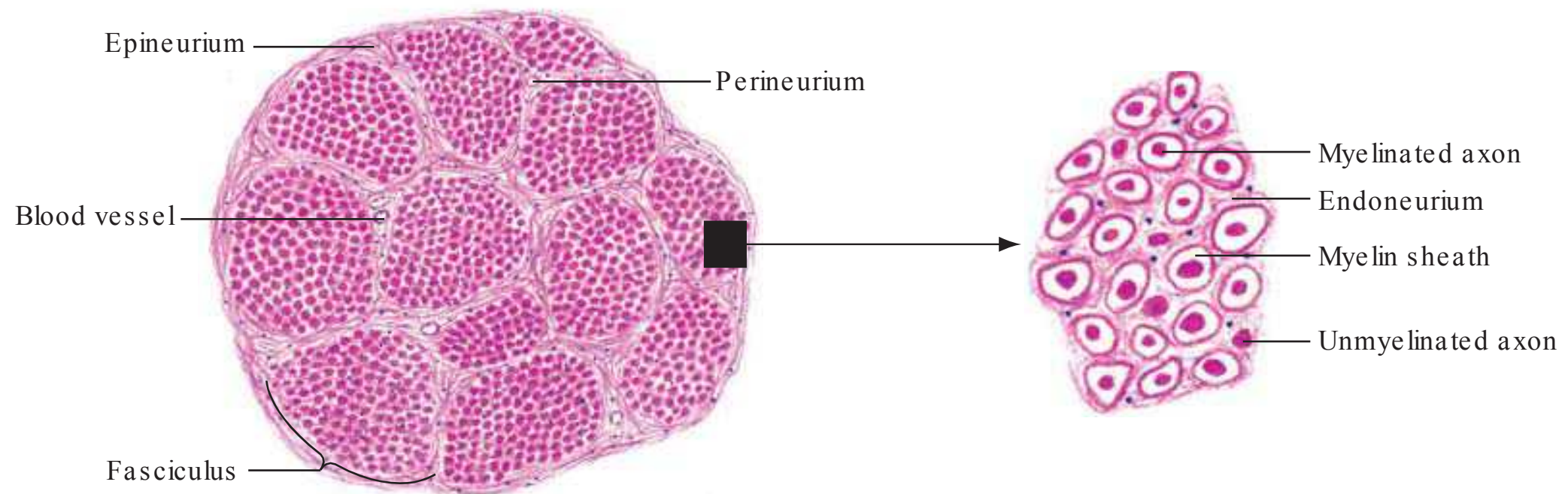
- Bundles of axons in the PNS are called peripheral nerves.
- These axons may belong to neurons of somatic or autonomic nervous system. These can be myelinated or unmyelinated or can be sensory, motor or mixed (Fig. 8.9).

- Cell bodies of motor neurons are in the CNS (Fig. 8.9) or in the autonomic ganglia. Cell bodies of sensory neurons are in the dorsal root ganglia or in the trigeminal ganglia. (For further details about the organisation of the nerve fibres, refer Neuroanatomy textbooks). Hence, nuclei present in sections of peripheral nerves will be of Schwann cells or fibroblasts (fibroblasts are present in the connective tissue of the nerves).
- In the peripheral nerve, each nerve fibre with its Schwann cell and basal lamina is enclosed in a thin sheet of connective tissue called endoneurium, that is the basal lamina is surrounded by endoneurium (Figs 8.9 and 8.10).
- Many nerve fibres together form fasciculus, which is enclosed in connective tissue layer called perineurium.
- Several such fasciculi are surrounded by a layer of connective tissue called epineurium.
- Epineurium, perineurium and endoneurium have blood vessels which supply the nerve fibres.
- In osmium-stained preparation, myelin sheath stains black (Fig. 8.11).

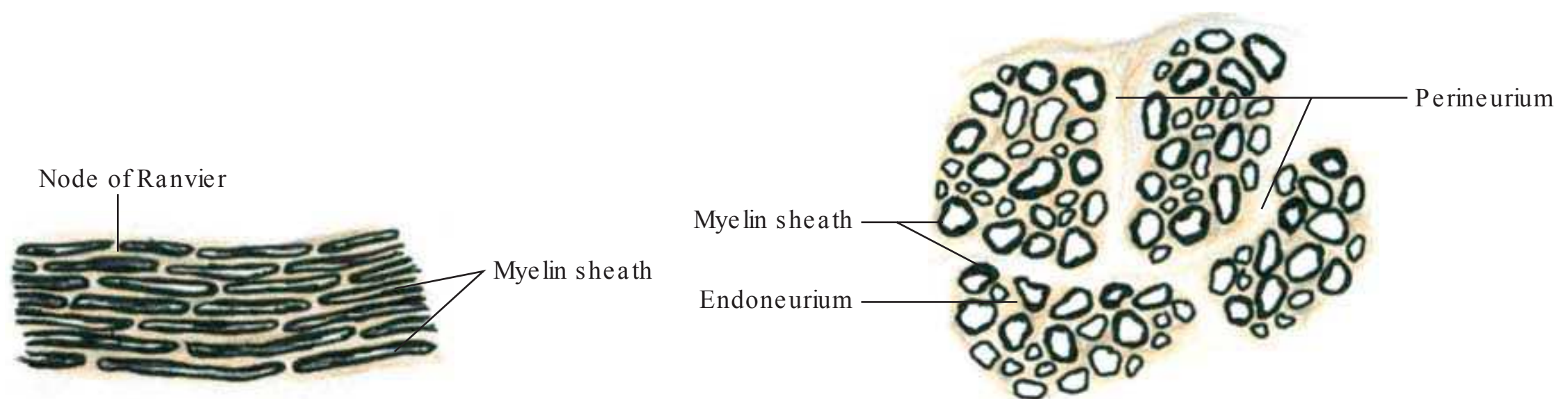


**Figure 8.9** Diagram showing (a) the sensory and motor neurons and (b) the organisation of peripheral nerve.





**Figure 8.10** Transverse section of peripheral nerve. Inset shows a portion of nerve in high magnification. (H&E pencil drawing)



**Figure 8.11** Osmium-stained preparation of peripheral nerve in (a) longitudinal and (b) transverse section. Myelin sheath (black stained) surrounding the axon can be seen. (Drawing)

## GANGLIA

- Ganglia (singular: ganglion) are collections of cell bodies of neurons present outside the CNS.
- They are of two types: spinal and autonomic.

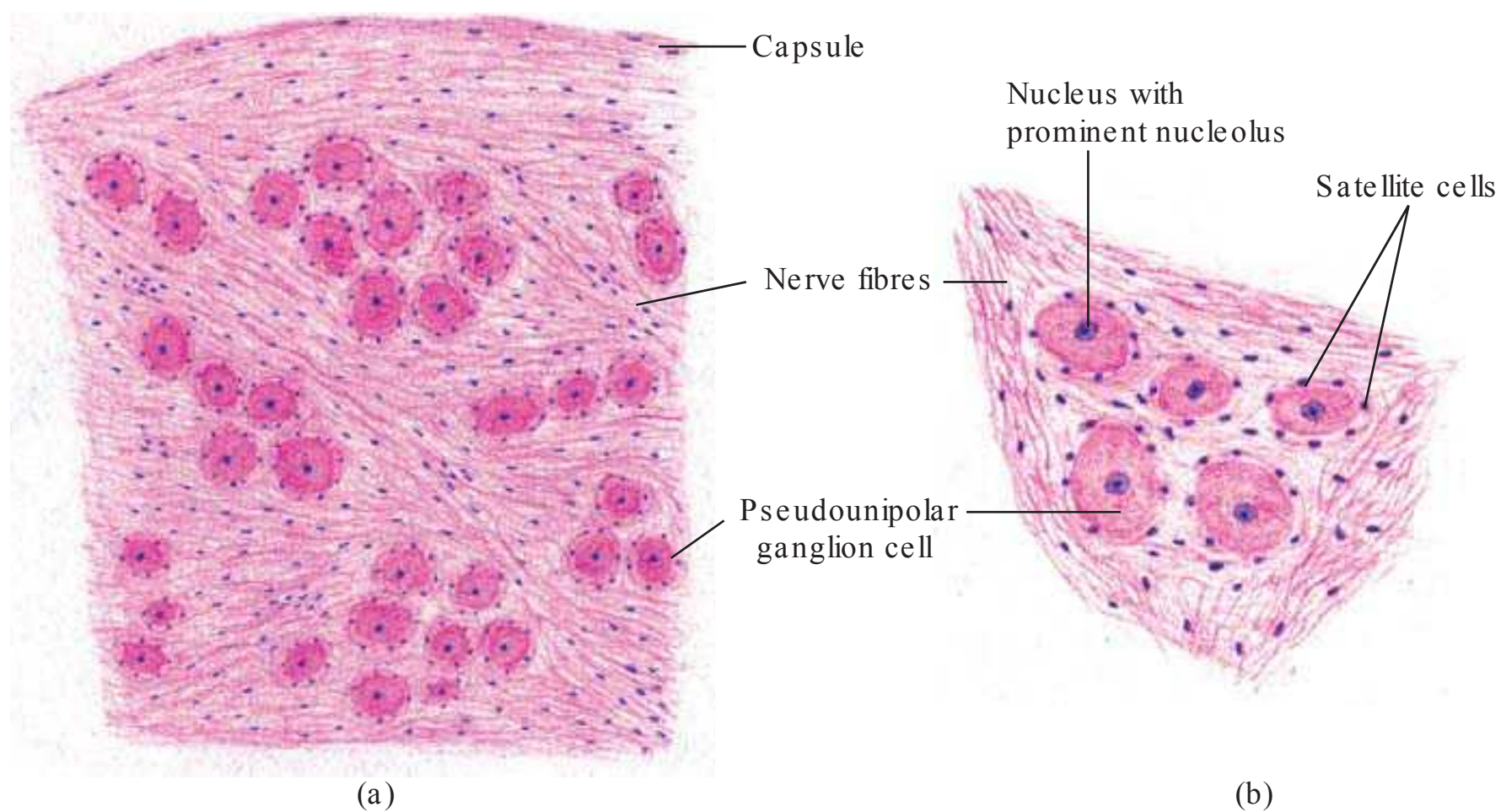
### SPINAL GANGLION (Fig. 8.12; PMG 8.1)

Spinal ganglion is present in the course of the dorsal root of spinal nerves (Fig. 8.9).

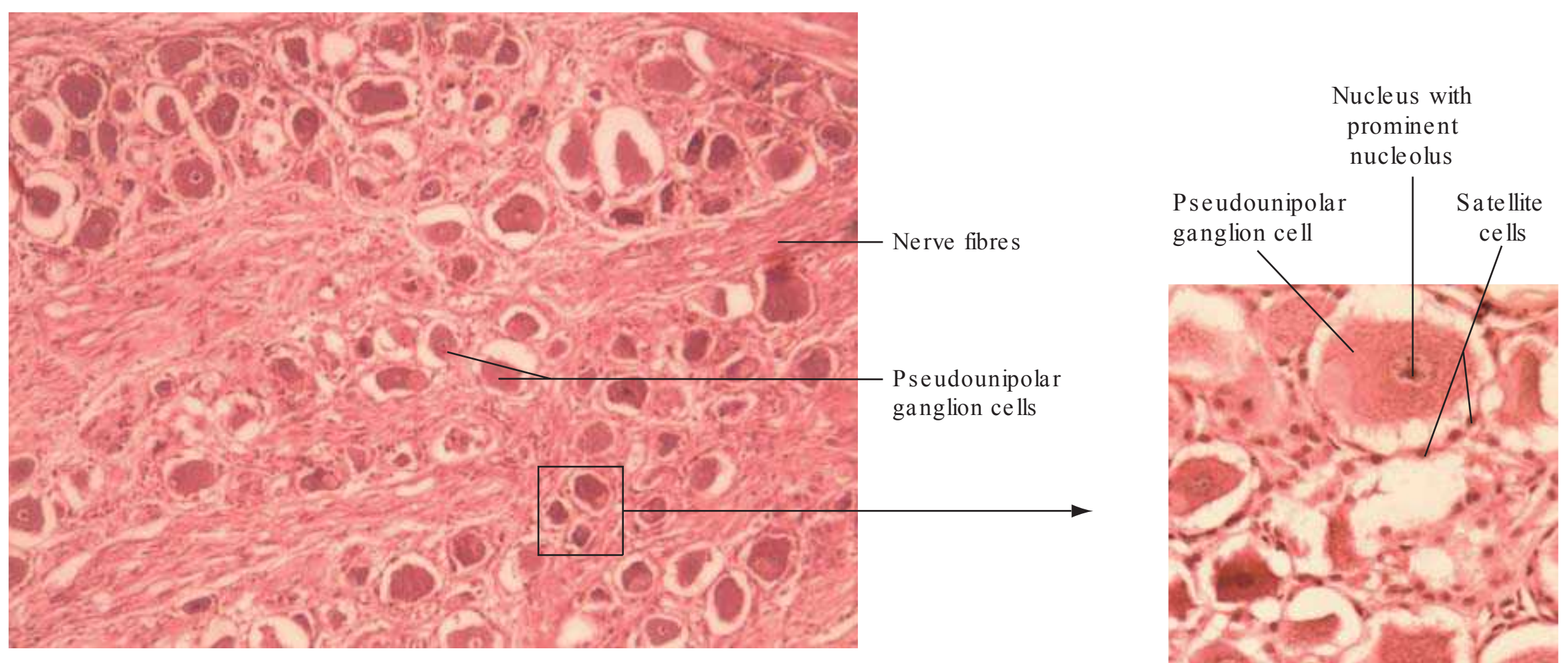
#### Microscopic Features

- The entire ganglion is covered by connective tissue capsule. Each ganglion is an aggregation of cell bodies of pseudounipolar neurons; some nerve fibers also pass through them.
- Each cell body is surrounded by a single layer of flat cells called satellite cells. Satellite cells provide structural support to the cell body. Nucleus of cell body is large with prominent nucleolus.





**Figure 8.12** Section of spinal ganglion in (a) low and (b) high magnification (H&E pencil drawing).



**PMG 8.1** Spinal ganglion (X10). Inset showing a further magnified view of spinal ganglion (X20). (H&E stain)

### **AUTONOMIC GANGLION** (Figs 8.13 and 8.14; PMG 8.2)

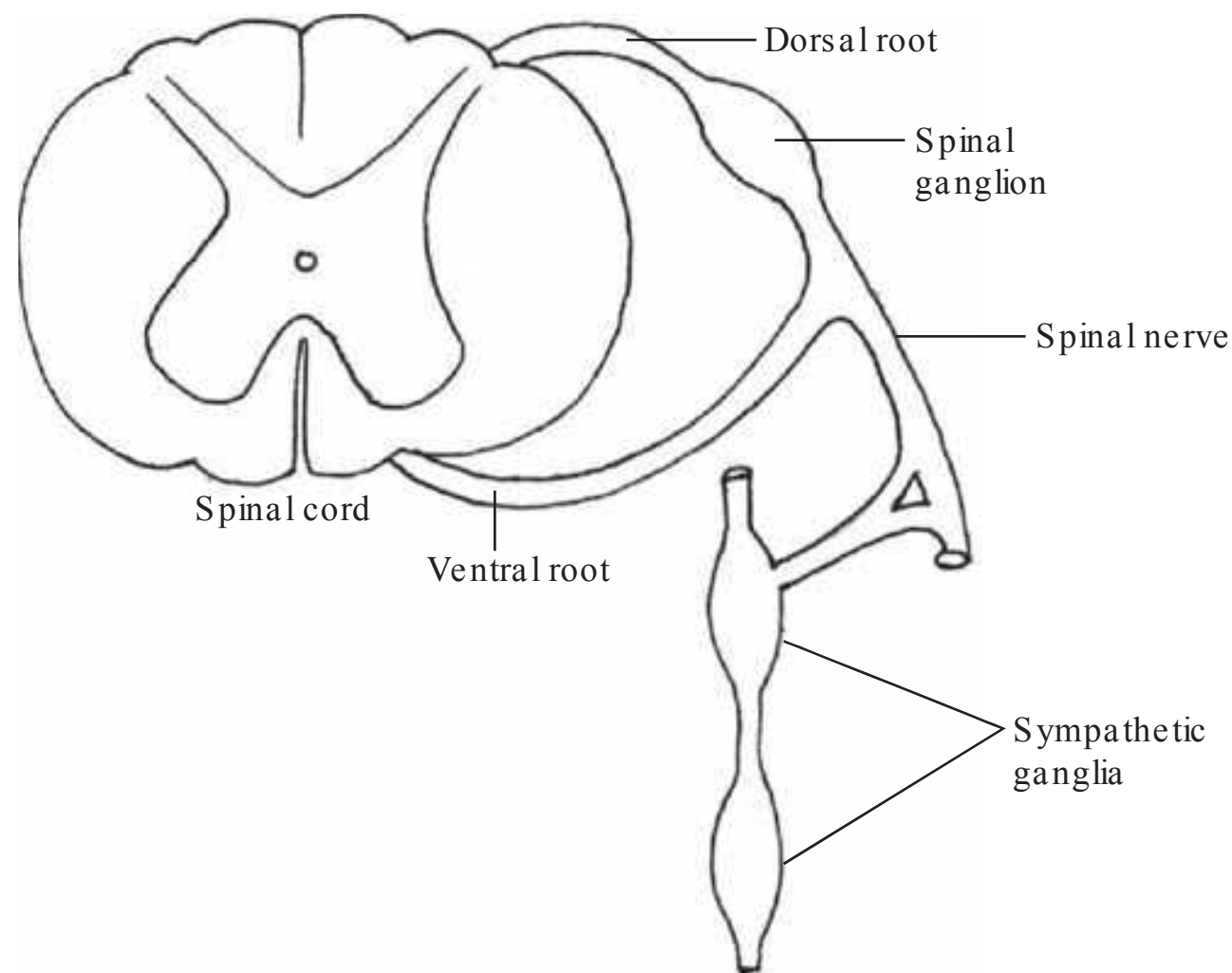
The sympathetic ganglia are present in the sympathetic chain (Fig. 8.13), whereas the parasympathetic ganglia are located close to the organs to which they supply.



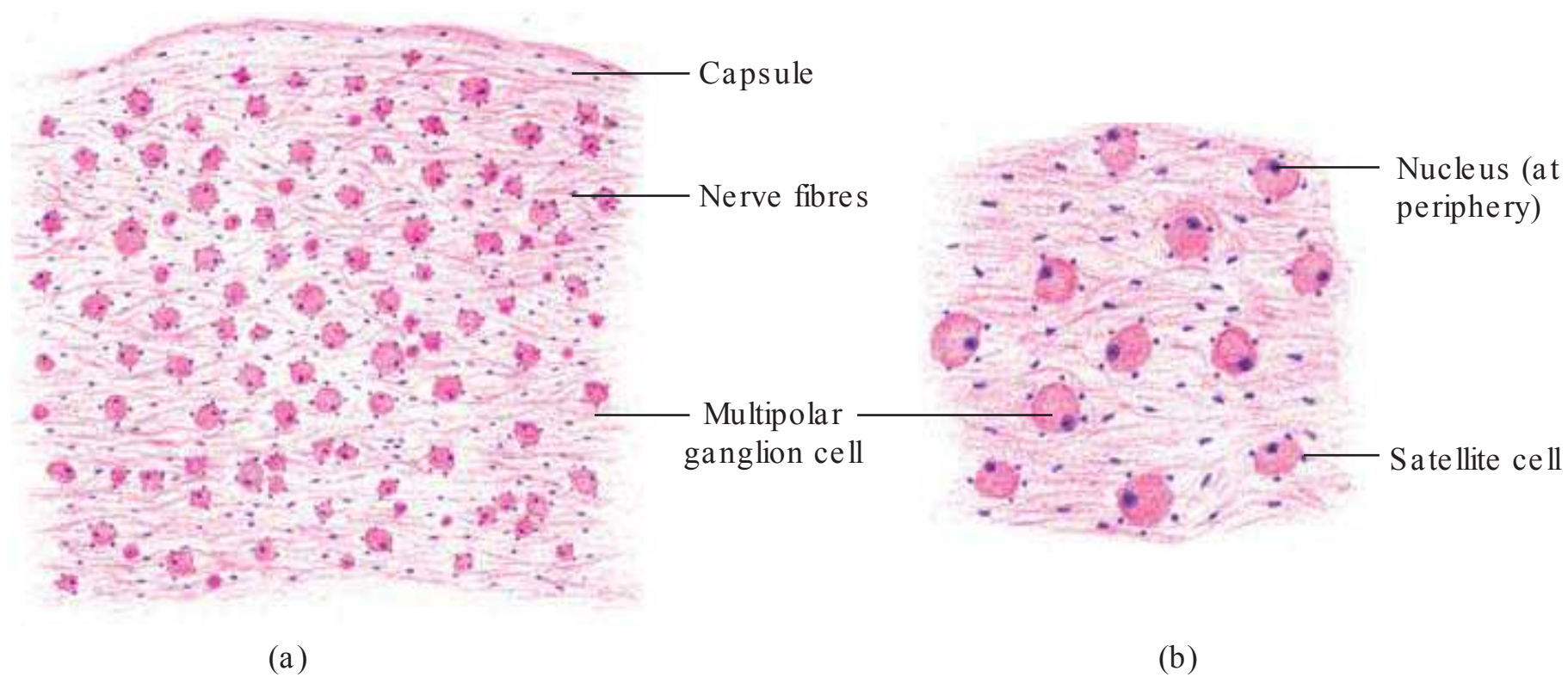
### Microscopic Features

- Similar to spinal ganglion, autonomic ganglion also has a capsule.
- It contains cell bodies of multipolar neurons. Size of cell bodies is smaller than cell bodies of spinal ganglion. Nucleus is large and eccentric in position. Satellite cells surround the cell body.
- Numerous dendrites and nerve fibres are present in between the cell bodies.

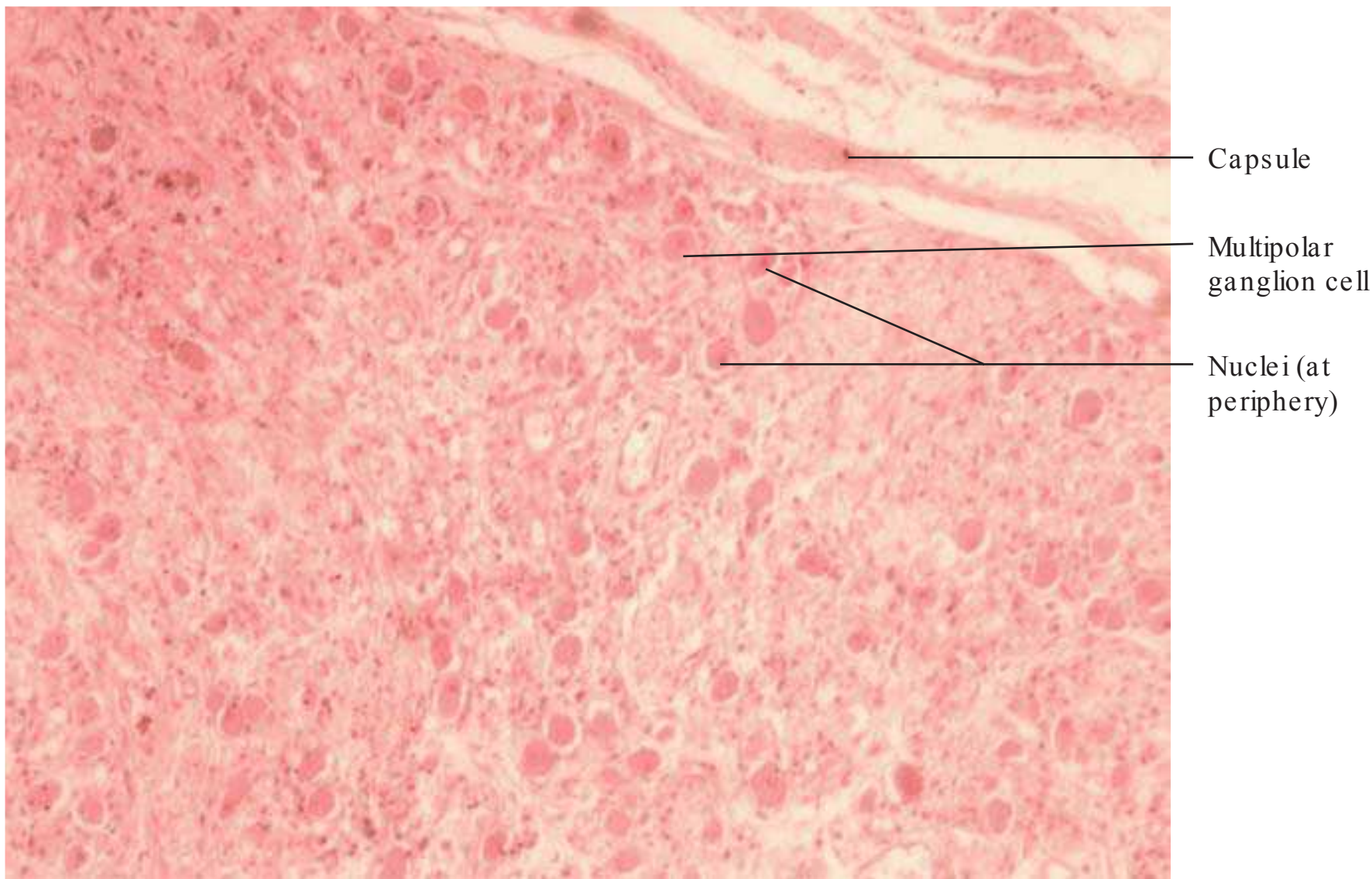
The differentiating features of spinal and autonomic ganglia are mentioned in Table 8.1.



**Figure 8.13** Sympathetic trunk.



**Figure 8.14** Section of sympathetic ganglion in (a) low and (b) high magnification (H&E pencil drawing).



**PMG 8.2** Sympathetic ganglion (H&E stain, X10).

**Table 8.1** Comparison of Spinal and Autonomic Ganglion

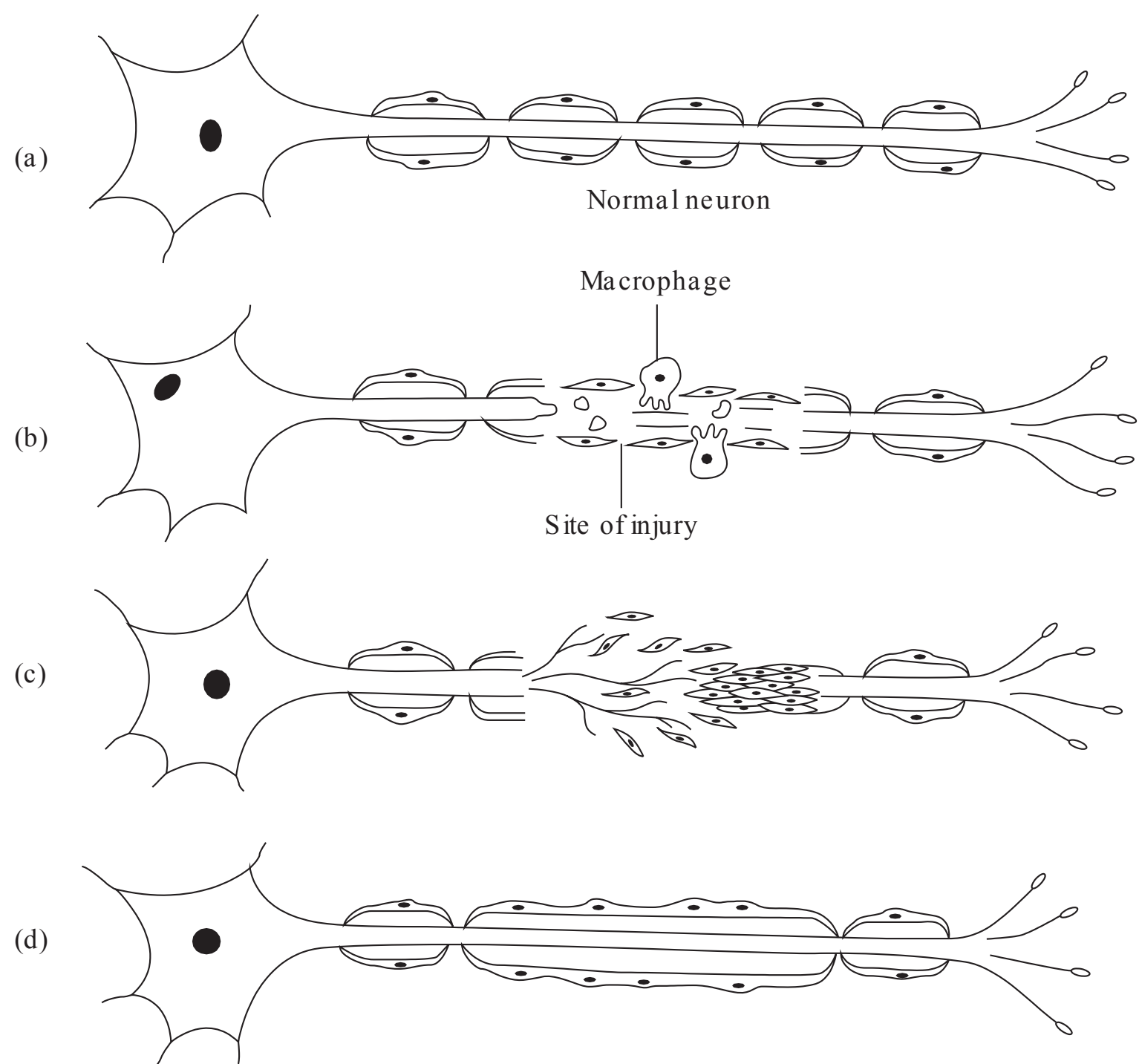
	Spinal	Autonomic
Cell bodies	Large, closely placed	Small, widely placed
Position of nucleus	Central	Eccentric
Satellite cells	More in number	Less in number

## RESPONSE OF NERVE TISSUE TO INJURY

The nerve tissue may be injured at the cell body or axon; damage to the cell body results in death of a neuron. However, injury to the axon results in the following changes:

- Injury to the axon causes degeneration in both proximal and distal segments of the axon (Fig. 8.15b).
- In distal segment, axon and myelin sheath undergo degeneration (Wallerian degeneration). Subsequently, degenerated tissue is removed by macrophages (Fig. 8.15b).
- Degeneration occurs in the proximal segment also (retrograde degeneration) (Fig. 8.15b), but it extends for only a few internodal segments. In the cell body, the nucleus moves to periphery and disappearance of Nissl bodies (chromatolysis) is observed.
- Regeneration begins with the proliferation of Schwann cells. Schwann cells proliferate and bridge the gap between the two damaged ends (Fig. 8.15c). Numerous small processes sprout from the proximal segment of the axon. The sprouting process passes through the Schwann cell column and re-establishes the continuity of the axon (Fig. 8.15c and d).
- Successful regeneration depends upon the amount of axoplasm lost due to injury; loss of large amount of axoplasm causes death of the axon.





**Figure 8.15** Response of nervous tissue to injury.

## CLINICAL CORRELATES

### Multiple Sclerosis

- This is an autoimmune disease in which there is destruction of myelin in the CNS. It can cause motor paralysis and loss of coordination and sensation; the symptoms depend upon the area of CNS involved in the disease.

### Schwannoma

- These are benign tumours arising from Schwann cells.

## KEYPOINTS

### Types of Neuron (Fig. 8.3)

Types of neuron	Examples
Multipolar	Motor neurons
Bipolar	Neurons in retina and olfactory cells of nasal mucosa
Unipolar (or pseudounipolar)	Neurons in dorsal root ganglia

Glial Cells (Fig. 8.4)

Types of glial cells	Functions
Astrocytes: These are of two types — protoplasmic and fibrous astrocytes	They take part in blood–brain barrier
Oligodendroglia (Fig. 8.7)	These are responsible for myelination of axons in the CNS
Microglia	These are phagocytic cells
Ependymal cells	These are responsible for production of cerebrospinal fluid

Peripheral Nerve (Figs 8.9 and 8.10)

- Bundles of axons in peripheral nervous system form peripheral nerve.
- These axons may belong to neurons of somatic or autonomic nervous system. These axons can be myelinated or unmyelinated, sensory or motor or mixed.
- The connective tissues associated with the peripheral nerve are epineurium, perineurium and endoneurium.

Ganglia

Type of ganglion	Type of neurons present
Spinal (Fig. 8.12; PMG 8.1)	Aggregation of cell bodies of pseudounipolar neurons
Autonomic (Fig. 8.14; PMG 8.2)	Aggregation of cell bodies of multipolar neurons

Also refer Table 8.1 for comparison between the two types of ganglia.

SELF-ASSESSMENT

1. Describe the structure of a neuron.
2. What are the different types of neurons? Give examples for each.
3. Compare the microscopic features of spinal and autonomic ganglia.
4. Describe the different types of glial cells and their functions.



# Muscle Tissue

- Muscle tissue is one of the four basic tissues (the other three basic tissues are the epithelial, connective and nervous tissues). It is a tissue specialised for contraction.
- The muscle cells develop from mesoderm.
- It is interesting to note that the nomenclature of some cell organelles in muscle is different from the one in other cells. Plasmalemma is called sarcolemma, cytoplasm is called sarcoplasm and endoplasmic reticulum becomes sarcoplasmic reticulum.
- Structurally, muscles are of two types:
  - (a) Smooth muscles, which lack striations.
  - (b) Striated muscles, which have striations. Striated muscles are further of two types, skeletal and cardiac muscles.

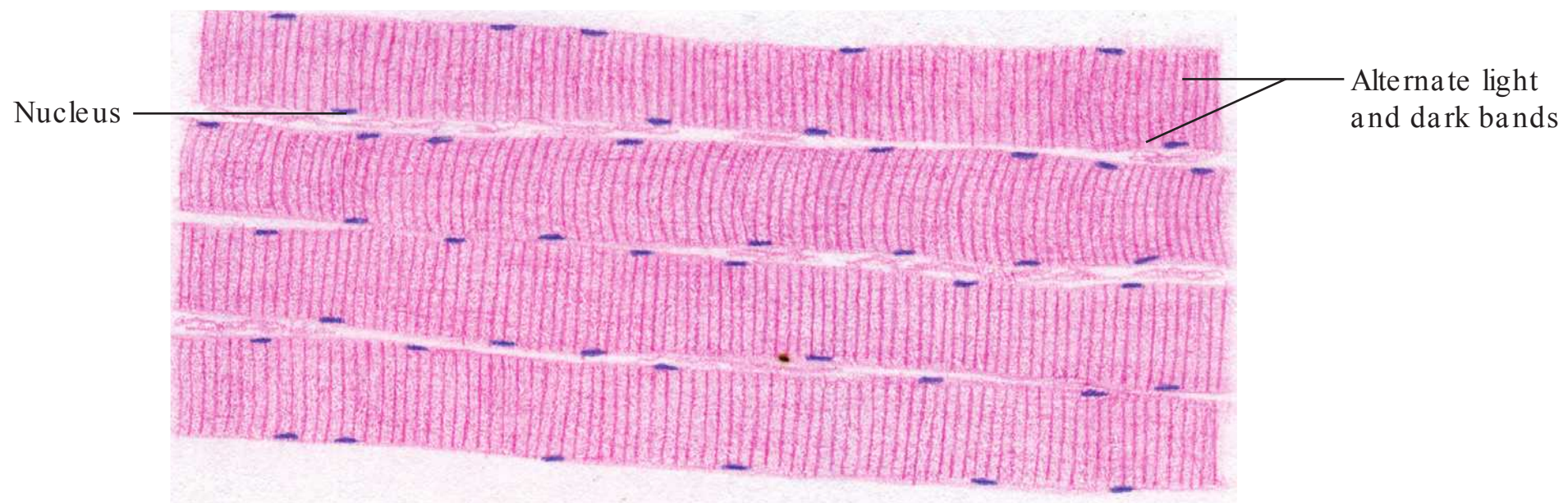
## SKELETAL MUSCLE

- Skeletal muscles have striations; hence they are also called striated muscles.
- They are mainly found in association with bones and are responsible for voluntary contraction; hence they are also called voluntary muscles.
- They are innervated by somatic nerves.

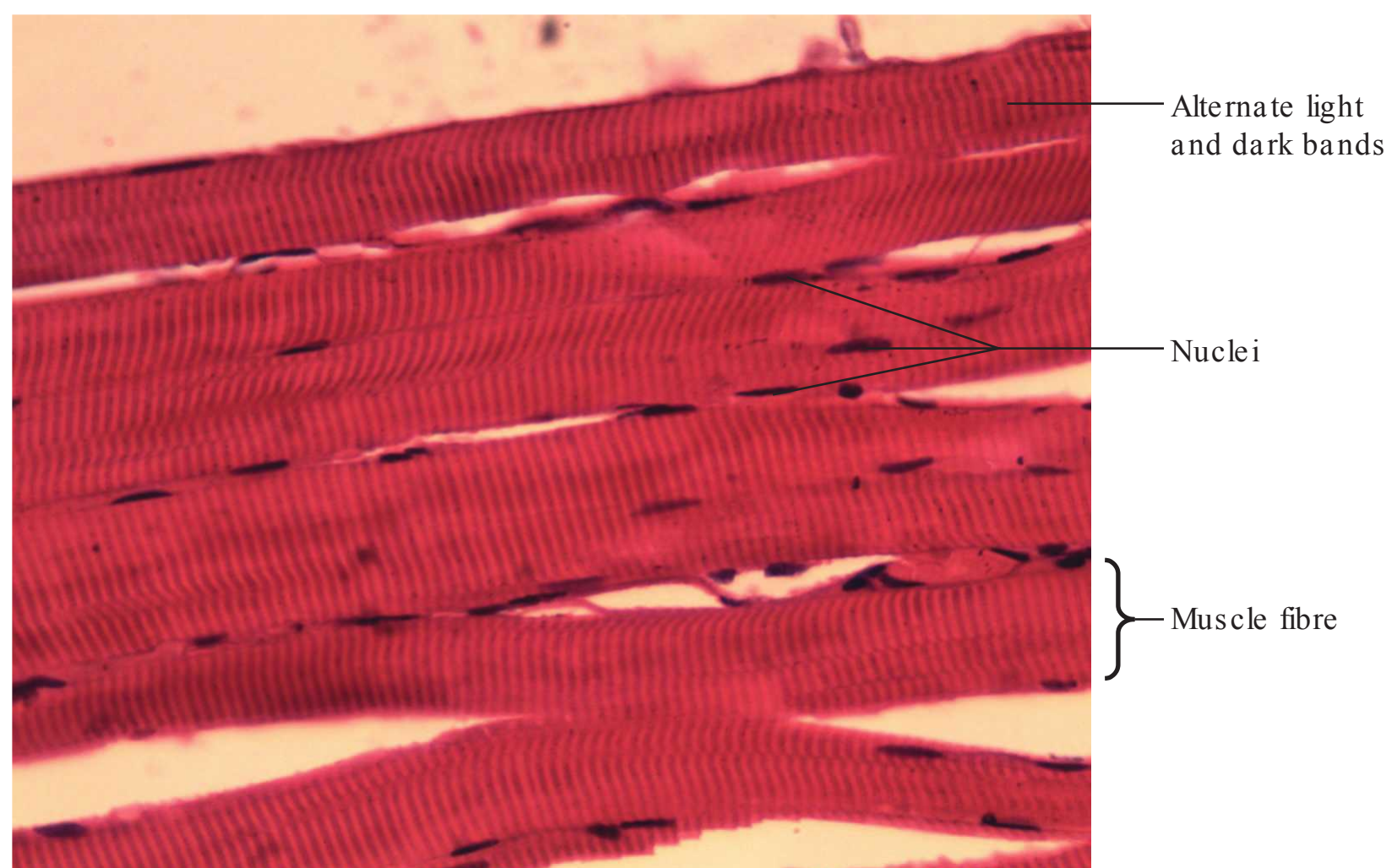
### MICROSCOPIC FEATURES OF SKELETAL MUSCLE CELLS (OR FIBRES)

- Skeletal muscle cells are derived from myoblasts. During the development, numerous myoblasts fuse together to form multinucleated muscle cells. Skeletal muscle cells are also referred to as skeletal muscle fibres.
- These are cylindrical, unbranched, multinucleated cells. The nuclei are flat and are located at the periphery of the cell.
- Each muscle fibre is surrounded by an external lamina which is similar to the basal lamina of epithelia. Outside the external lamina, there is a network of reticular fibres. The external lamina together with reticular fibres forms the endomysium. The endomysium can be seen in the cross-sectional view of skeletal muscle, discussed subsequently.
- Longitudinal section of skeletal muscle fibres shows cross-striations. These cross-striations consist of alternating dark and light bands—dark bands are called A bands and light bands are called I bands (Fig. 9.1; PMG 9.1). 'A' stands for anisotropic and 'I' for isotropic, referring to the optical properties of the muscle viewed under polarised light microscopy.





**Figure 9.1** Longitudinal section of skeletal muscle in high magnification. Unbranched fibres with striations can be seen—nuclei are fat and at the periphery (H&E pencil drawing).



**PMG 9.1** Longitudinal section of skeletal muscle (H&E stain, X40).

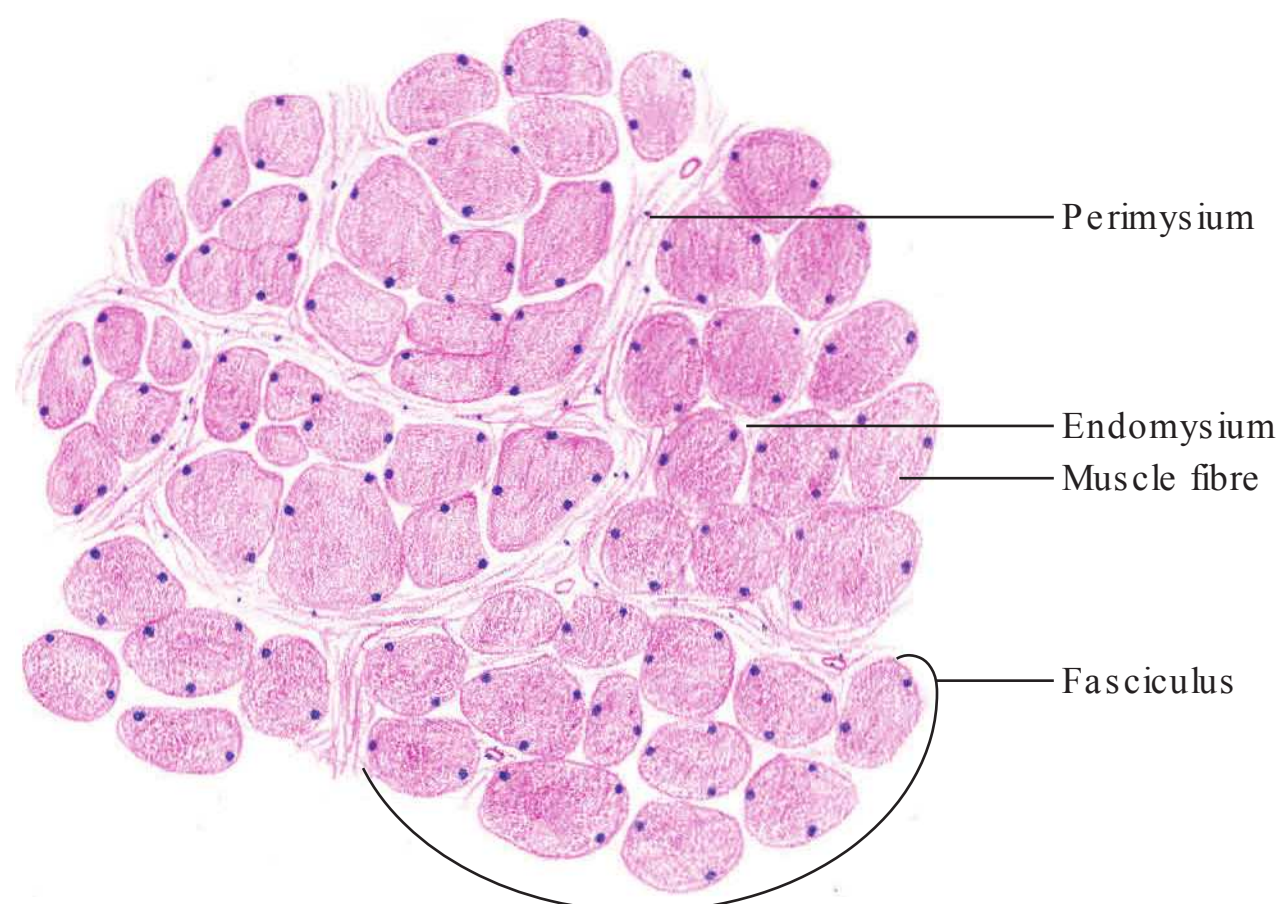
### Organisation of Skeletal Muscle

- As mentioned previously, individual muscle fibre is surrounded by connective tissue called endomysium (Fig. 9.2). It consists of the external lamina and reticular fibres.
- The individual muscle fibres are grouped as small bundles called fasciculi (singular: fasciculus).
- Each fasciculus is surrounded by connective tissue called perimysium (Fig. 9.2). Muscles are bundles of many fasciculi, and the entire muscle is covered by connective tissue called epimysium.
- As the connective tissue enters the muscle, it brings blood vessels and nerves along with it, which supply the muscle fibres.
- The connective tissue coverings are also illustrated in Figure 9.3, which shows the organisation and ultrastructural details of skeletal muscle.

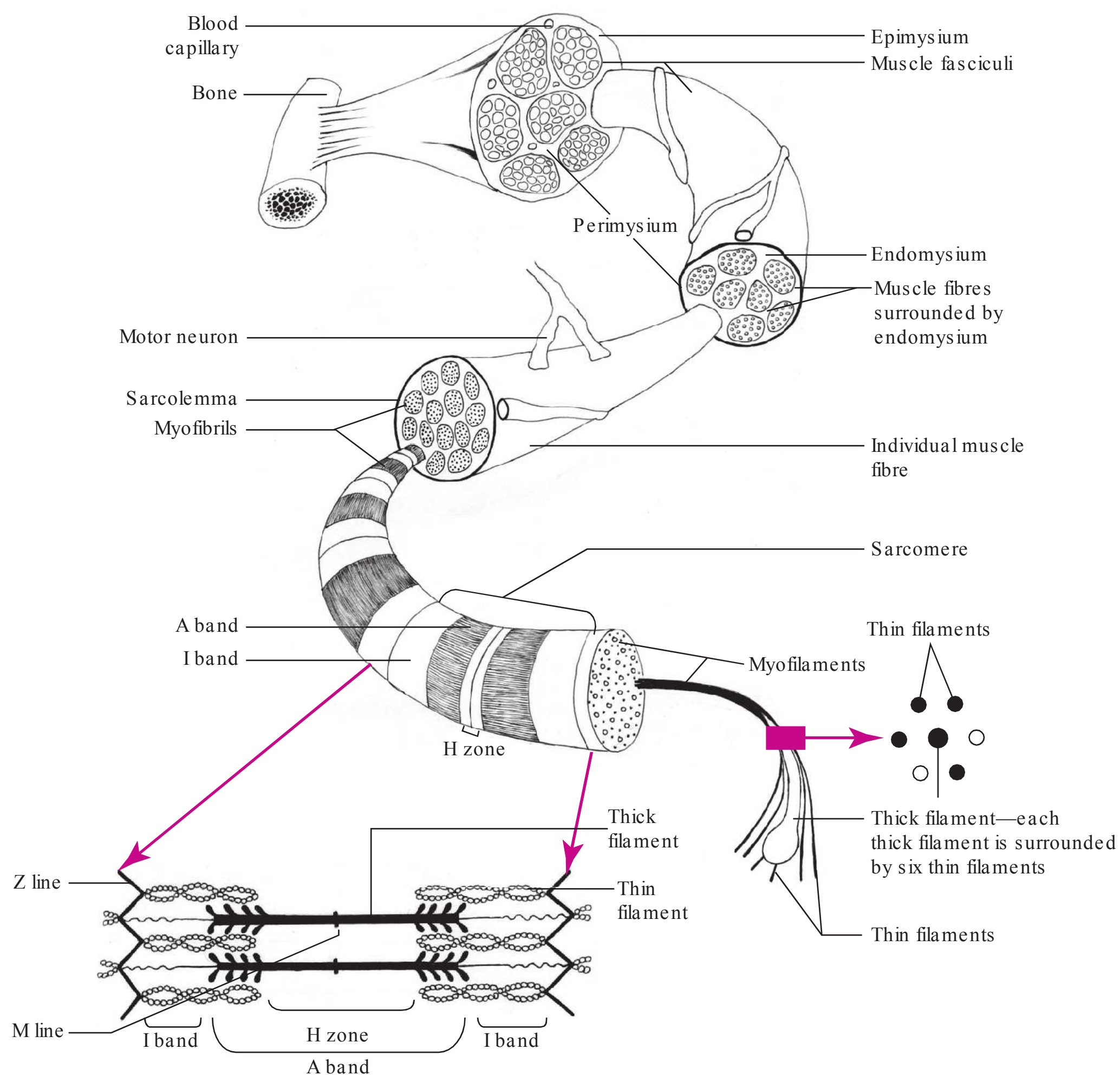
### ULTRASTRUCTURE OF SKELETAL MUSCLE FIBRE

An individual skeletal muscle fibre is a bundle of myofibrils present in its sarcoplasm (Fig. 9.3). It should be noted that these are ultrastructural details and can be seen under electron microscopy.





**Figure 9.2** Cross-section of skeletal muscle in high magnification. Multinucleated muscle fibres are seen (H&E pencil drawing).



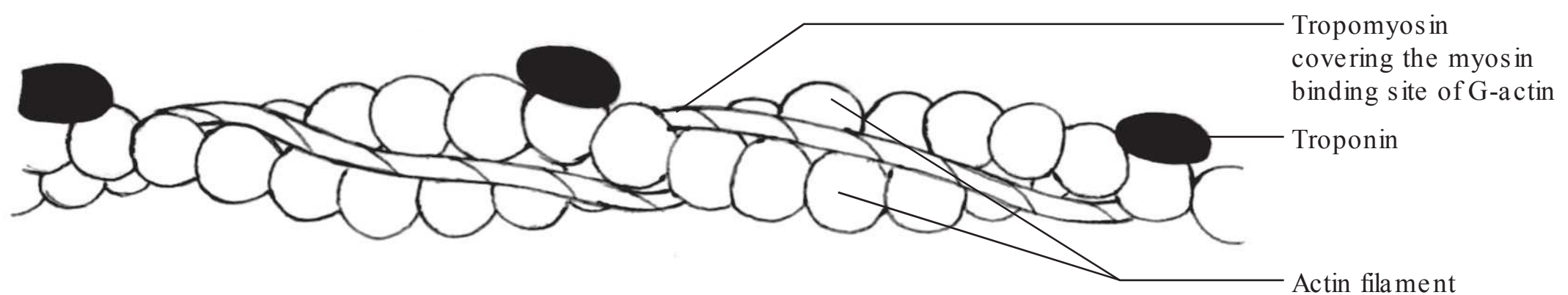
**Figure 9.3** Organisation of skeletal muscle fibres with their components.

### Myofibrils (Fig. 9.3)

- Myofibrils are unbranched, contractile threads, arranged parallel to each other, along the long axis of muscle fibre.
- Each myofibril has alternating I and A bands—bisecting the light I band is a thin dark line called Z band.
- These bands of adjacent myofibrils are aligned transversely and this arrangement gives cross-striations to the skeletal muscle.
- Each myofibril consists of longitudinally oriented protein filaments called myofilaments.

### Myofilaments

- There are two types of myofilaments in skeletal muscle: thick and thin filaments (Fig. 9.3).
- Thick filaments are composed of the protein myosin.
- Thin filaments are composed of three types of proteins: actin, tropomyosin and troponin. Interaction between the actin and myosin proteins brings about muscle contraction. Troponin regulates the actin–myosin interaction and hence the muscle contraction. It consists of three subunits: troponin T, I and C (Fig. 9.4). Troponin T binds with tropomyosin, troponin I inhibits the interaction between actin and myosin and troponin C binds with calcium ions.
- The organisation of myofilaments is described under sarcomere.



**Figure 9.4** Thin filament and its components.

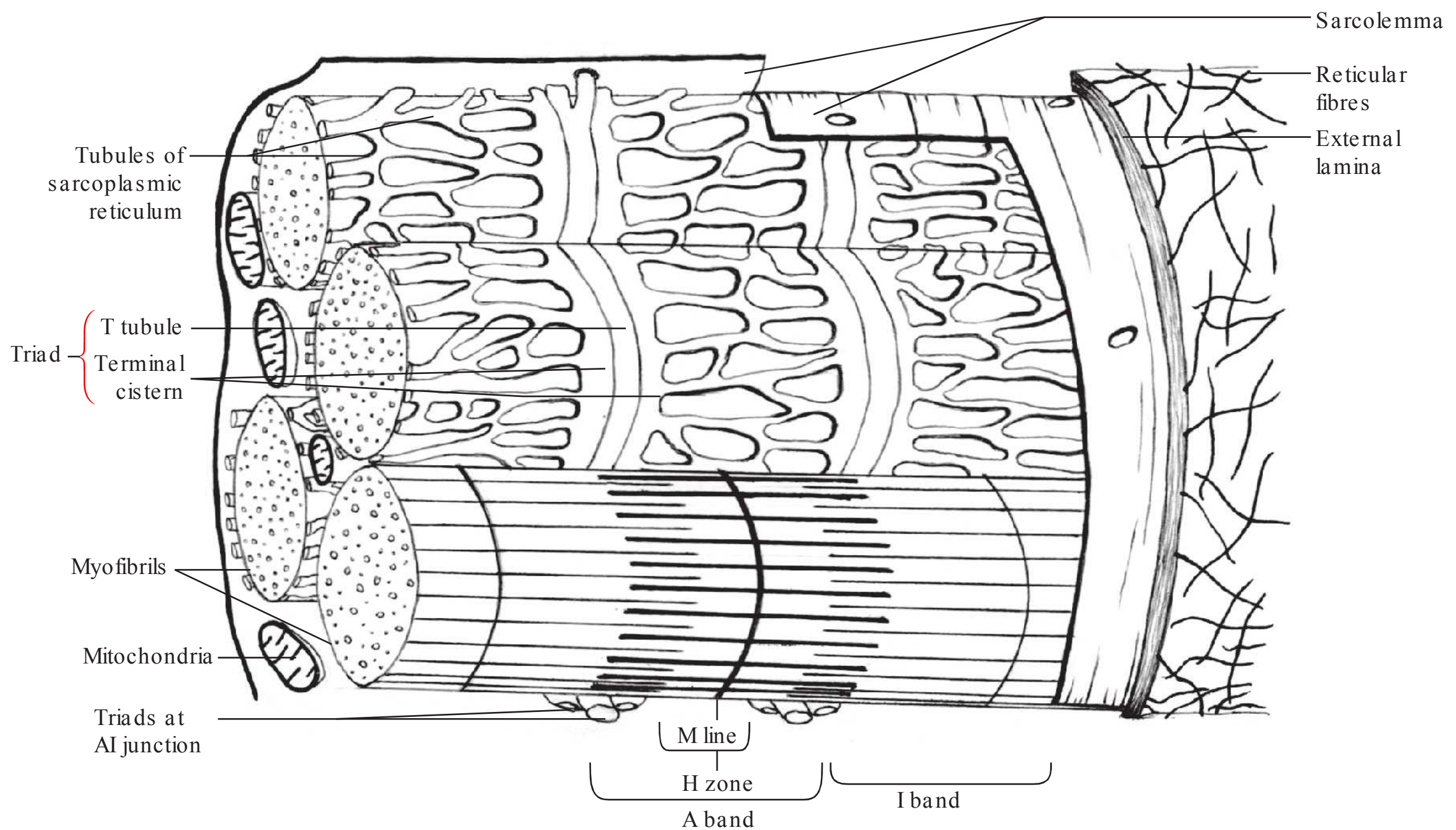
### Sarcomere (Fig. 9.3)

- A segment of myofibril between the two adjacent Z lines is called sarcomere. It is the contractile unit of the muscle, and it shortens when the muscle contracts.
- I bands contain only thin filaments.
- The A band is present in the centre of a sarcomere. It contains thick filaments and part of thin filaments overlapping with thick filaments. Each thick filament is surrounded by six thin filaments.
- When the muscle is relaxed, a lighter H band is seen in the centre of the A band. In the region of H bands, the thin filaments do not overlap the thick filament.
- A thin dark line, the M line, is seen in the middle of the H band, and it is the site where two adjacent myosin filaments are connected.

### Triads

- At the AI junction, the three tubes constitute a triad, one T tubule in the centre and one terminal cistern on either side of the T tubule (Fig. 9.5). Triads play an important role in muscle contraction.
- The T tubule is invagination of the sarcolemma into the muscle cell.
- The sarcoplasmic reticulum forms a tubular network that surrounds the myofibril; at the AI junction, on both sides of the T tubule, the sarcoplasmic reticulum expands to form terminal cisternae (Fig. 9.5). Terminal cisternae contain high calcium concentration.

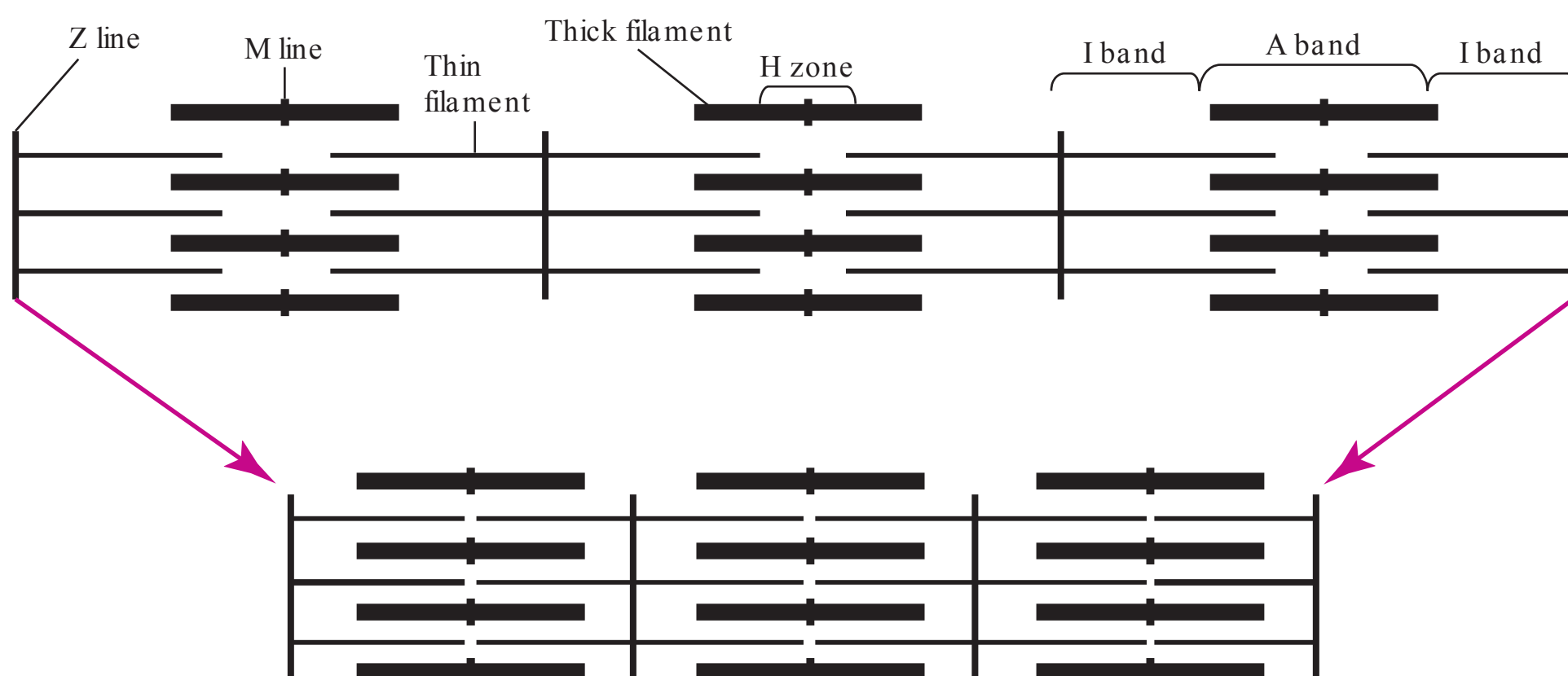




**Figure 9.5** Schematic diagram showing the ultrastructure of a muscle fibre. Sarcolemma has been partly removed and four myofibrils can be seen. At the A-I junctions, triad can be seen which consists of T tubule in the centre and a terminal cistern on either side of it.

### CONTRACTION OF SKELETAL MUSCLE (Fig. 9.6)

- Actin has myosin-binding site. In the relaxed state, tropomyosin binds with the myosin-binding site of actin and troponin I inhibits the interaction between actin and myosin.
- The action potential from the nerve depolarises the sarcolemma at the myoneural junction.
- The action potential is carried into the cell through the T tubules.
- Calcium ions are released from the terminal cisternae into the sarcoplasm.
- Calcium ions, released in the sarcoplasm, bind with troponin C and result in a conformational change which causes the tropomyosin to shift, and thus the myosin-binding site on the actin is exposed.



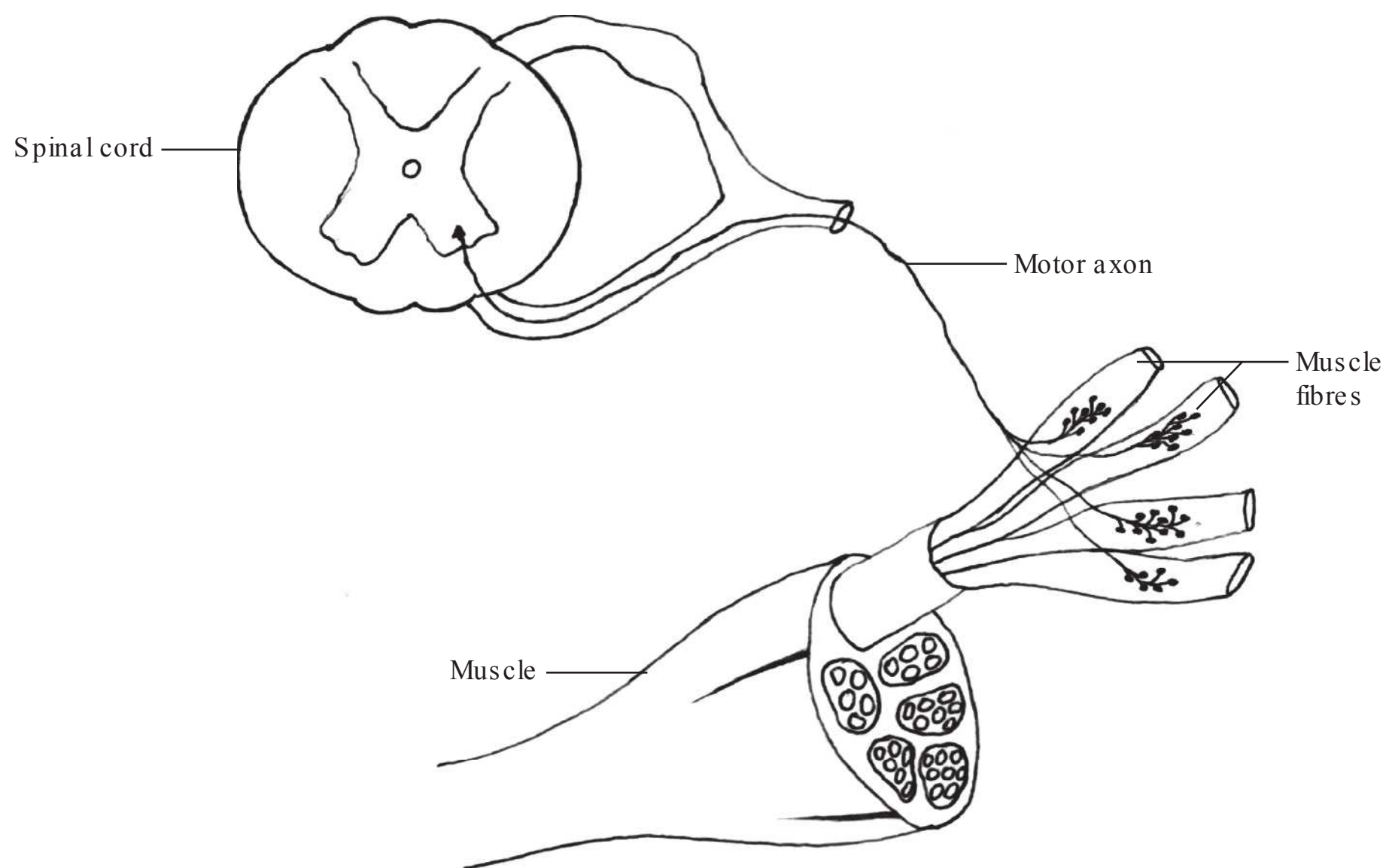
**Figure 9.6** Schematic presentation of a sarcomere in relaxed (top) and contracted (bottom) skeletal muscle.

At the same time, troponin I moves away from actin. The exposed myosin-binding sites on the actin are now available for interaction with myosin. (See Fig. 9.4 for the structure of thin filament.)

- The myosin binds with the actin.
- ATP binds with myosin and gets hydrolysed, resulting in the release of energy.
- Conformational changes in the myosin result in the movement of myosin and pull the actin filaments towards the M line.
- I and H bands become short, and Z discs move towards the centre of the sarcomere. This results in shortening of sarcomeres, leading to shortening of myofibrils and the entire muscle.
- The length of the thin and thick filaments does not change during muscle contraction.
- Relaxation occurs when the nervous stimuli stop. The calcium ions are removed from the sarcoplasm by sarcoplasmic reticulum through active transport. Calcium is removed from troponin C. TnI and tropomyosin return to their resting state, inhibiting the interaction between the actin and the myosin and covering the myosin-binding site on the actin, respectively.

### Neuromuscular Junction

- Each skeletal muscle fibre is innervated by a single motor axon. One axon innervates several muscle fibres, and all the skeletal muscle fibres innervated by the same axon are called a motor unit (Fig. 9.7).
- The neuromuscular junction is a synapse between the axon terminal of a motor neuron and the skeletal muscle fibre. It consists of a presynaptic membrane, a synaptic cleft and a postsynaptic membrane (Fig. 9.8).



**Figure 9.7** A motor unit.

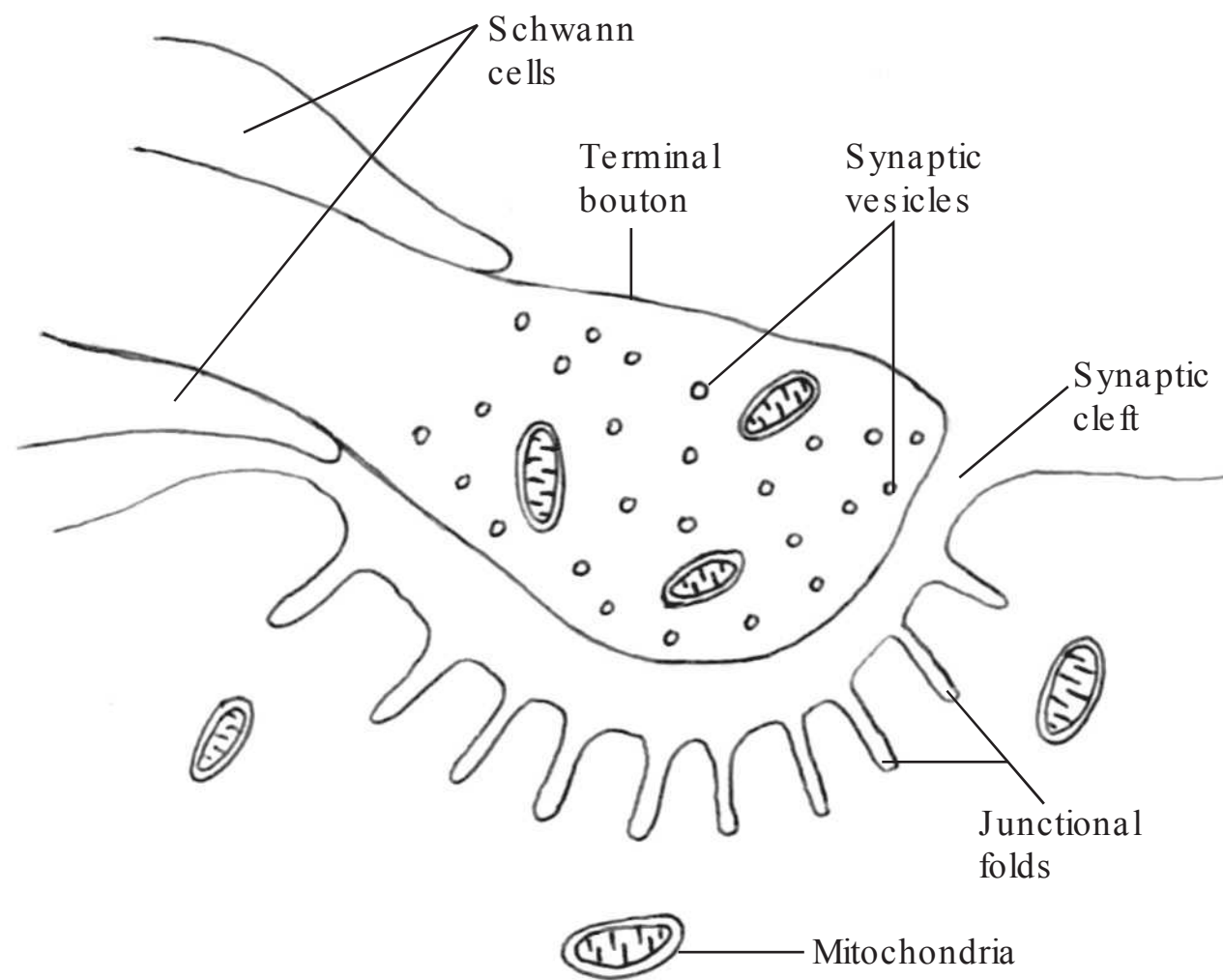
#### Presynaptic Membrane

- It is formed by the terminal bouton of the axon.
- The axon loses its myelin sheath at the axon terminal, but the Schwann cell is present on the non-synaptic surface of the terminal bouton.
- The terminal bouton contains numerous mitochondria and synaptic vesicles containing acetylcholine (a neurotransmitter).

#### Synaptic Cleft

- It is the area between the presynaptic membrane and the sarcolemma (postsynaptic membrane).





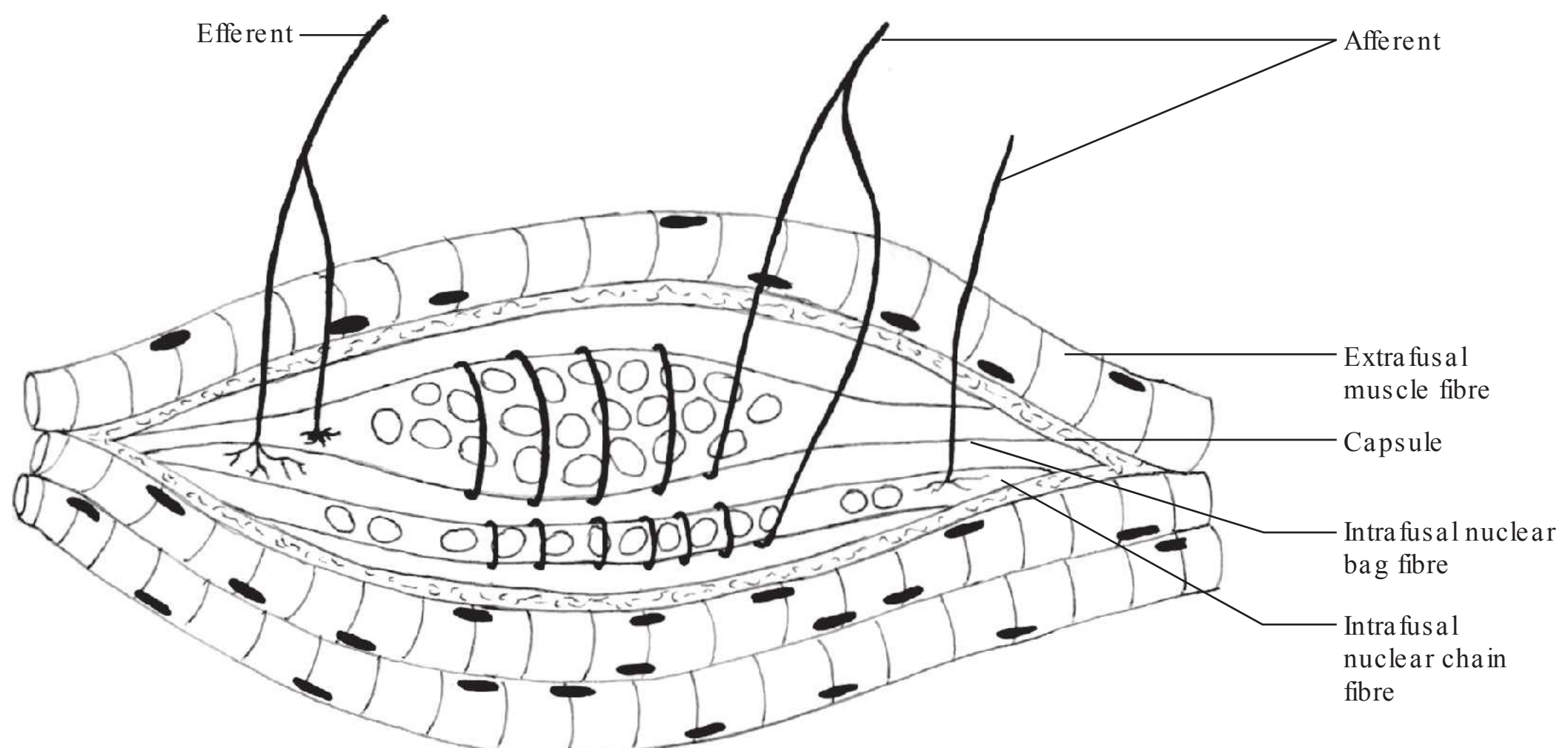
**Figure 9.8** Neuromuscular junction.

### *Postsynaptic Membrane*

- It is formed by the part of the sarcolemma of the muscle cell that is in closest proximity to the terminal bouton.
- At the junction, the sarcolemma forms numerous folds called junctional folds.
- Acetylcholine receptors are present on this membrane.

## **MUSCLE SPINDLE**

- Muscle spindles are proprioceptors present in the skeletal muscle.
- It is fusiform-shaped sensory receptor is composed of a connective tissue capsule which encloses a fluid-filled space containing a few modified muscle fibres (intrafusal fibres) (Fig. 9.9).



**Figure 9.9** Muscle spindle.

- There are two types of **intrafusal** fibres—some are thick and long (nuclear bag fibres) and some are thin and short (nuclear chain fibres).
- **Extrafusal** fibres are the normal contractile skeletal muscle fibres that surround the **intrafusal** fibres.
- When the muscle is stretched, the spindles are also stretched. This causes **reflex** contraction of the **extrafusal** fibres (stretch **reflex**).

### GOLGI TENDON ORGAN

- The Golgi tendon organ are proprioceptive receptors located in the tendons of the skeletal muscles near its insertion.
- They help to protect the muscles, tendons and ligaments from injury caused by overstretching.
- They consist of a connective tissue capsule enclosing strands of collagen fibres. The sensory nerve pierces the capsule and supplies the receptors.
- These receptors are stimulated by strong muscle contractions, and the impulse is carried by sensory neuron. The  $\alpha$ -motor neuron supplying the muscle is inhibited; as a result, the muscle relaxes.

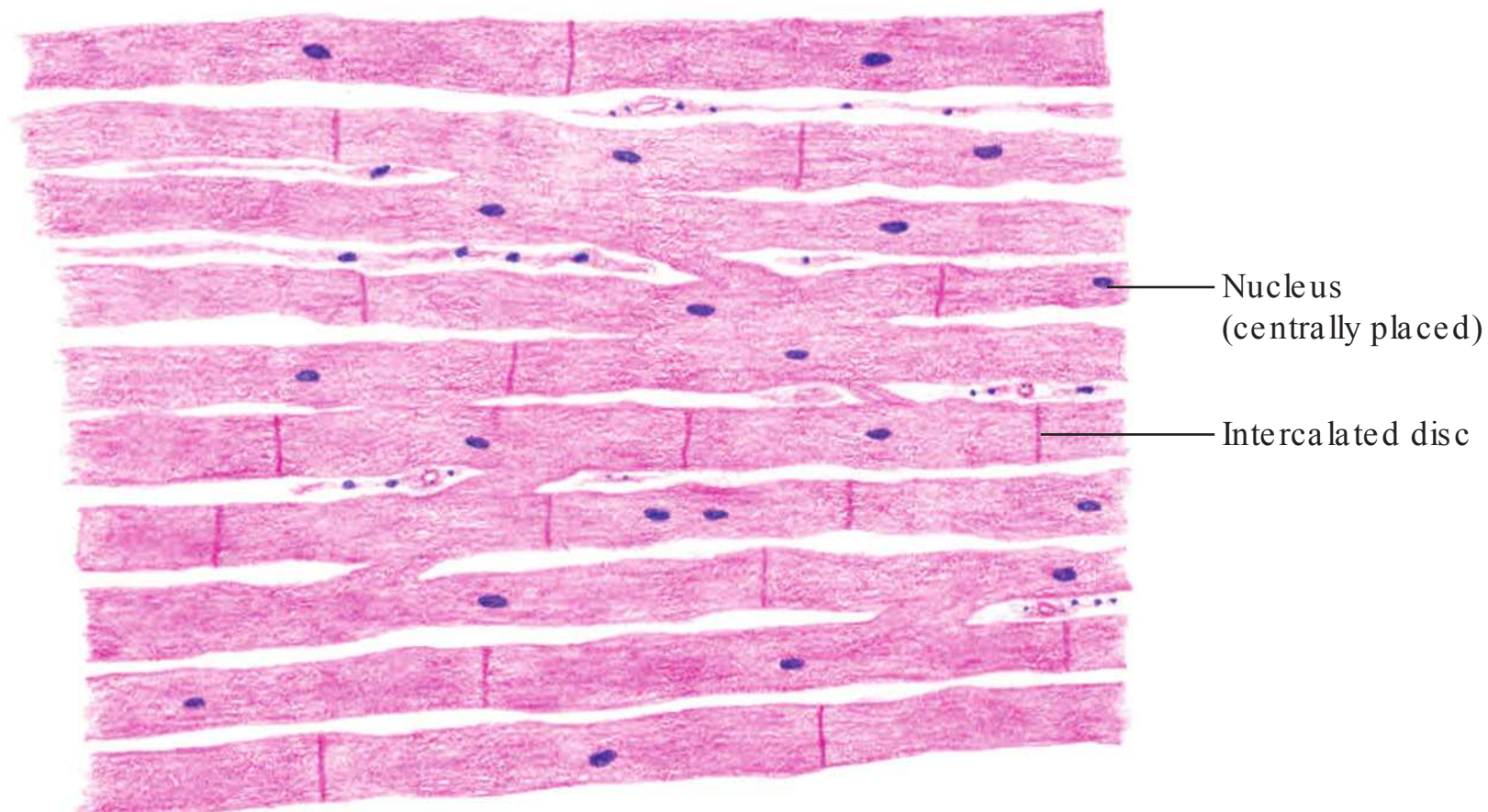
### MUSCLE-TENDON JUNCTION

- At the junction of the muscle and the tendon, the connective tissue of the muscle (epimysium, perimysium and endomysium) blends with the connective tissue of the tendon.
- At this junction, the muscles form invaginations of sarcolemma. The external lamina of the muscle fibres also enters these invaginations.
- The collagen fibres of the tendon also enter into the invaginations of the muscles and get attached with the external lamina.
- Inside the muscle cell, the actin filaments of the last sarcomere get attached to the sarcolemma.
- Hence, the force of contraction is transmitted from the last sarcomere to the sarcolemma, from sarcolemma to external lamina, then to the tendon and finally to the bone.

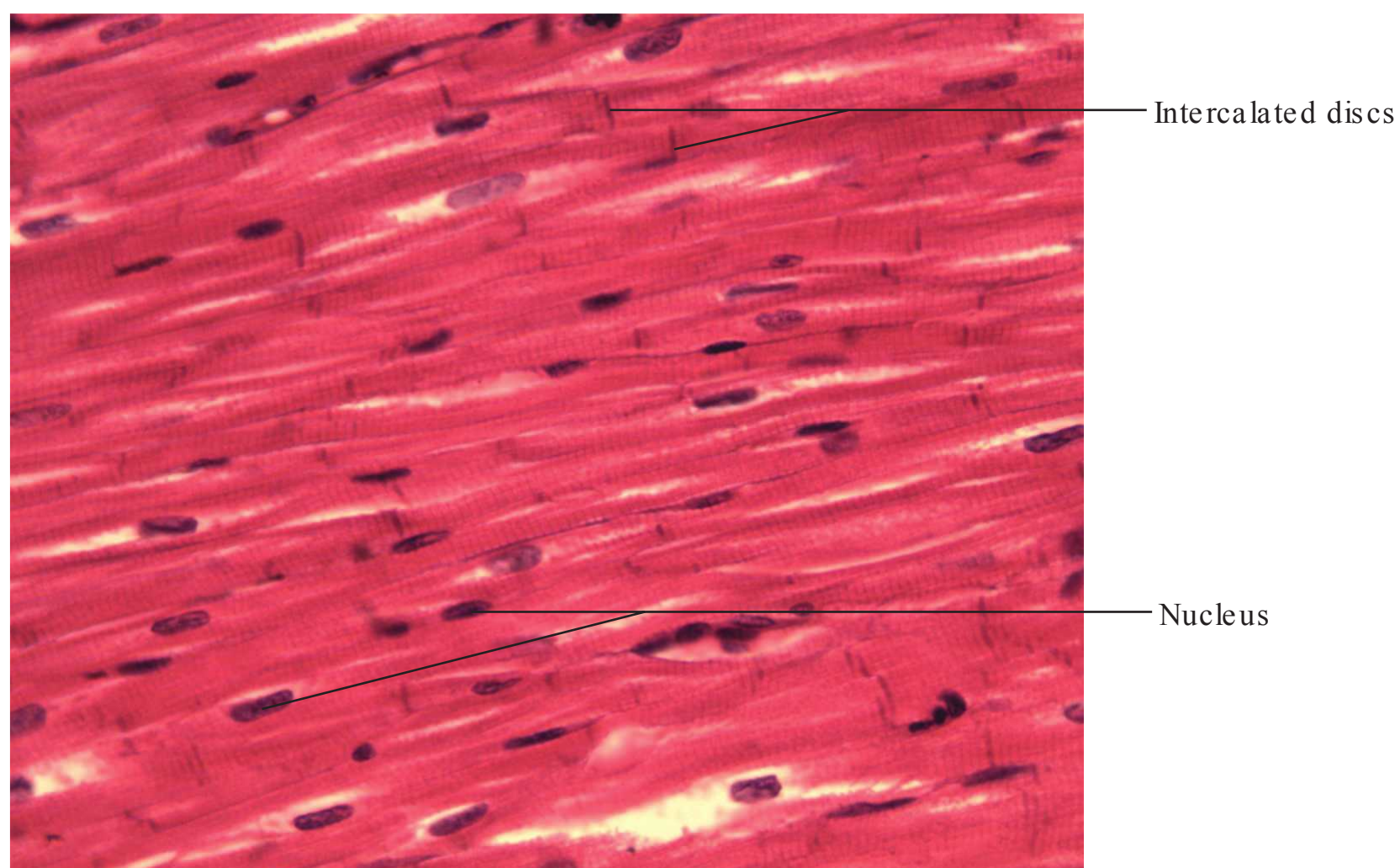
## **CARDIAC MUSCLE**

- Like the skeletal muscle, the cardiac muscle also has cross-striations (the striations in cardiac muscles are less prominent).
- The arrangement of the contractile proteins in the myofibrils is the same as skeletal muscle and gives rise to A, I, M, Z and H bands.
- The cardiac muscle differs from the skeletal muscle both functionally and structurally. The important features of the cardiac muscle which are different from the skeletal muscle are as follows:
  - (a) Cardiac muscle fibres branch and anastomose with the neighbouring muscle fibres (Fig. 9.10). They show intercalated discs (described later).
  - (b) They have centrally placed single (maybe two) nucleus per cell (Fig. 9.10; PMG 9.2).
  - (c) They have more mitochondria than skeletal muscles. Sarcoplasmic reticulum is not well organised. The cisterna of the sarcoplasmic reticulum is associated with the T tubule at Z discs; these two tubes contribute to the formation of dyads instead of triads (in skeletal muscle, at AI junction).





**Figure 9.10** Longitudinal section of cardiac muscle in high magnification. Branching fibres, centrally placed nucleus and intercalated discs can be seen (H&E pencil drawing).



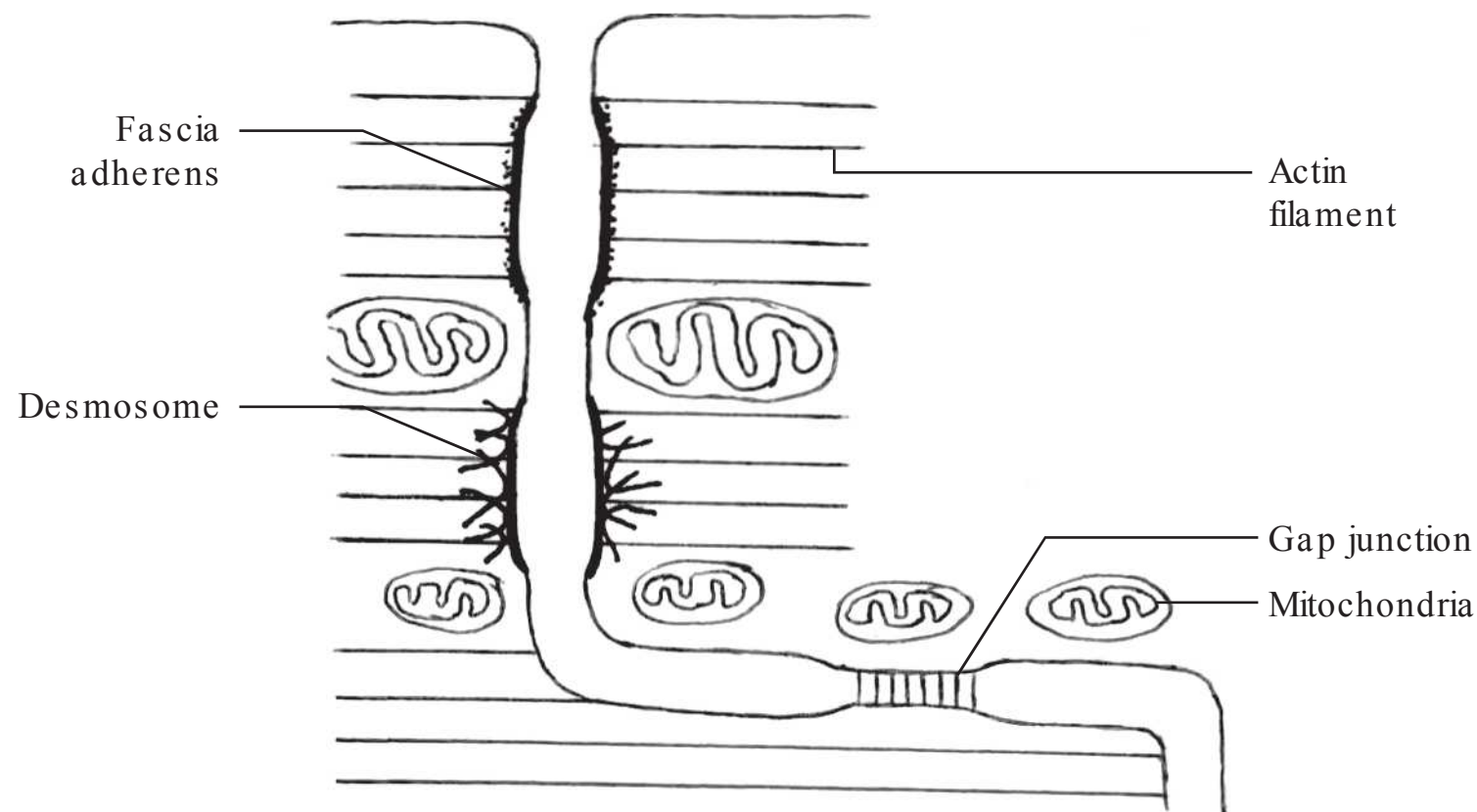
**PMG 9.2** Longitudinal section of the cardiac muscle (H&E stain, X40).

- (d) The cardiac muscle is involuntary in function. It is innervated by the autonomic nervous system, which regulates the heart rate.
- (e) There is no regeneration after damage.

### INTERCALATED DISCS

- Individual muscle cells join end to end by intercalated discs (PMG 9.2). Each disc is formed by the cell membranes of the adjacent muscle cells and their junctional complex.
- These discs have a step-like pattern with transverse parts oriented perpendicular to the myofibril and longitudinal parts oriented parallel to the muscle fibre.
- The junctional complex consists of three components: in the transverse parts of the discs are fascia adherens and desmosomes and in the longitudinal parts are gap junctions (Fig. 9.11).





**Figure 9.11** Structure of an intercalated disc.

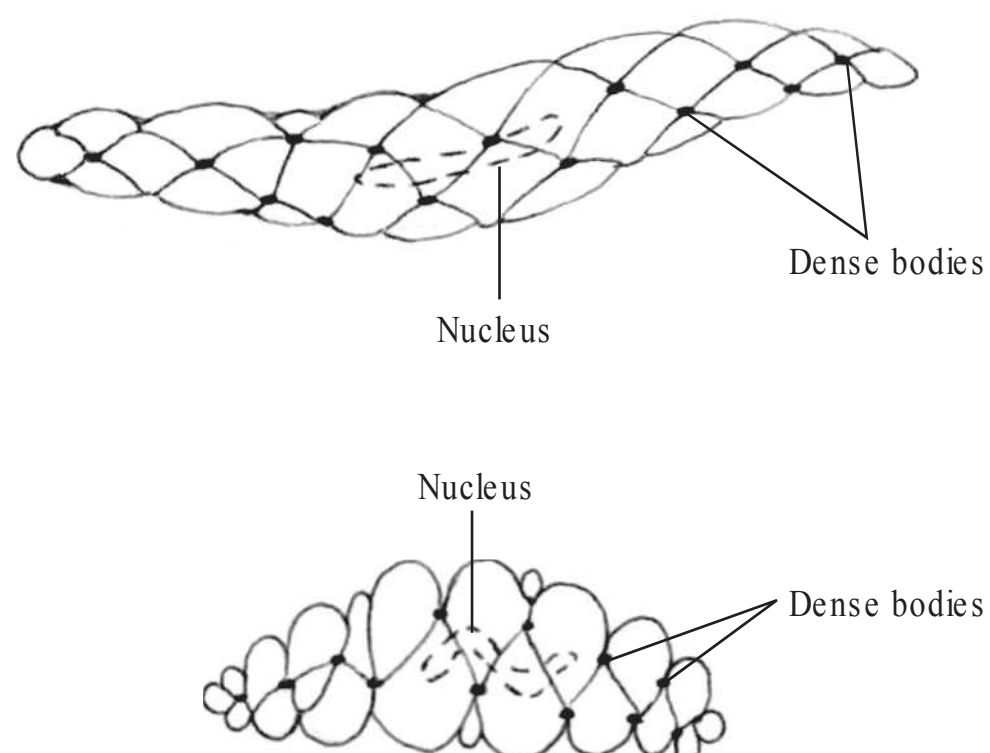
- Fascia adherens are similar to zonula adherens. Desmosomes are present below the fascia adherens in the transverse part of the discs.
- Gap junctions located in the transverse parts of the discs are responsible for the electronic coupling of the adjacent muscle fibres. They allow the action potentials to spread across the muscle fibres quickly by permitting the passage of ions between cells, producing rapid and synchronous depolarisation of the heart muscles. For this reason, the cardiac muscle is called a functional syncytium.

## SMOOTH MUSCLE

- Smooth muscles are present in the walls of hollow organs such as gastrointestinal tract, respiratory tract and urinary tract.
- These are involuntary muscles as they are innervated by the autonomic nervous system.
- These muscle cells divide actively and have capacity to regenerate.

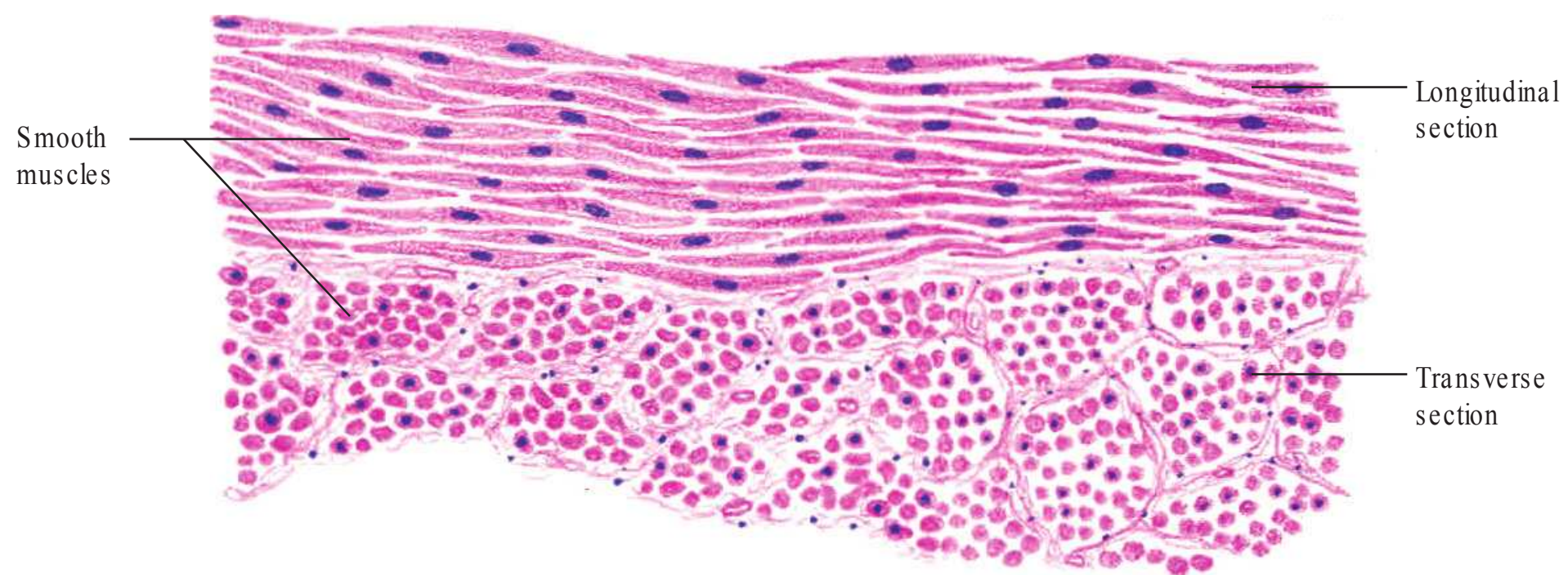
### MICROSCOPIC FEATURES OF SMOOTH MUSCLE CELLS (OR FIBRES)

- Smooth muscle fibres are spindle-shaped cells. Each muscle fibre has one elongated nucleus in the centre (Figs 9.12 and 9.13).
- Muscle cells are enclosed by the external lamina which is surrounded by a network of reticular fibres.



**Figure 9.12** Smooth muscles in relaxed (top) and contracted states (bottom). The muscle fibre is spindle shaped with an elongated nucleus.

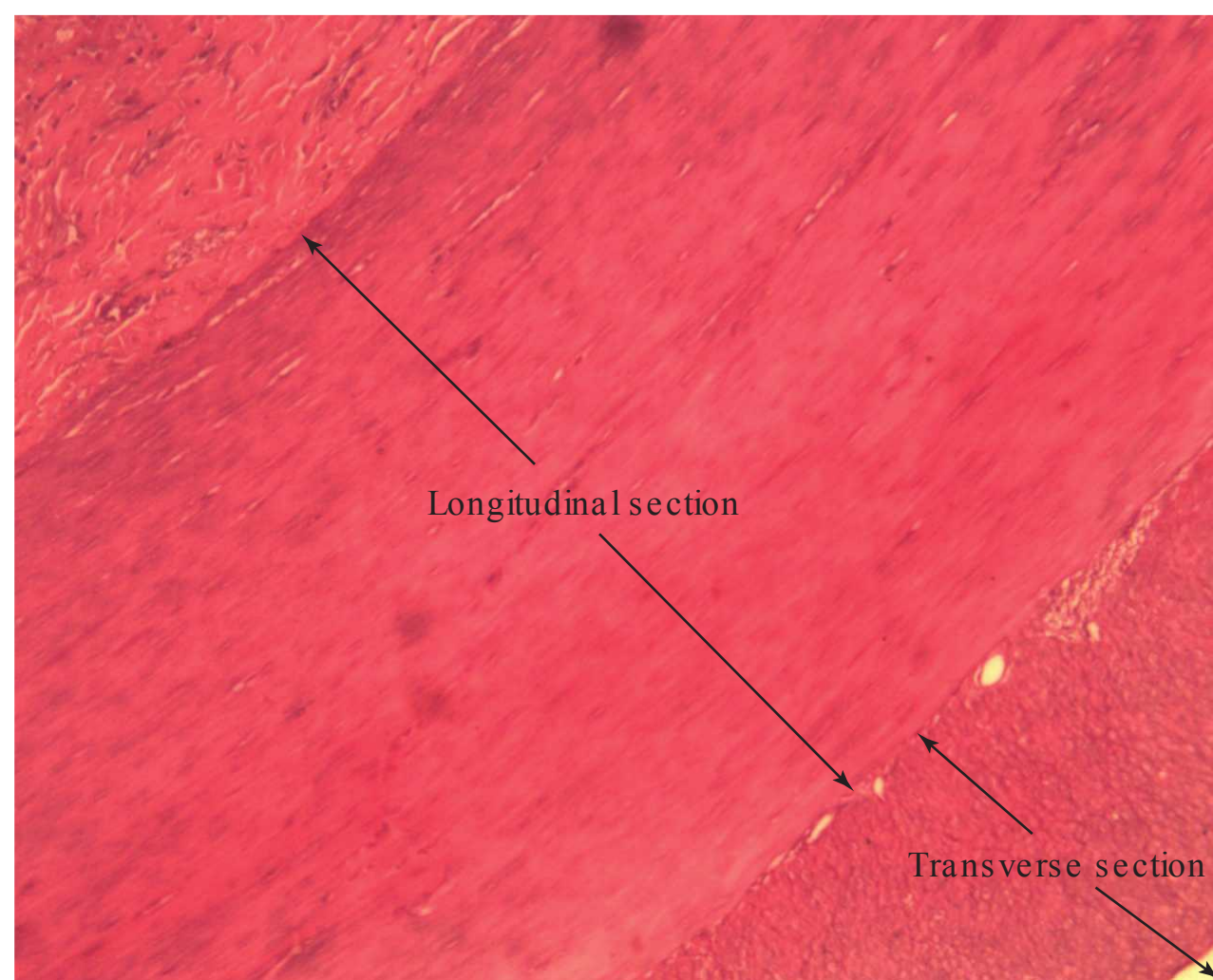




**Figure 9.13** Longitudinal and transverse sections of smooth muscle in low magnification.

### Organisation

- Usually, they are arranged in a circular or longitudinal manner (Fig. 9.13; PMG 9.3).
- Muscle cells are grouped together in fasciculi. Adjacent fasciculi are separated by thin connective tissue.
- Each fasciculus acts as a contractile unit.
- Within a fasciculus, muscle fibres run parallel to each other. Tapering ends of neighbouring muscle fibres overlap with each other.



**PMG 9.3** Longitudinal and transverse sections of smooth muscle (H&E stain, X10).

### ULTRASTRUCTURE OF SMOOTH MUSCLE CELLS

Electron microscopy reveals the ultrastructural details of smooth muscles.

#### Myofibrils

- Unlike the striated muscles, the myofibrils of the smooth muscle are not well organised (no myofibrils and sarcomere) and hence they are non-striated. T tubules are not present in smooth muscles.
- Myofibrils in the smooth muscles are oriented obliquely, criss-crossing the muscle cell.
- Myofibrils are attached to the anchoring points on the cell membrane called dense bodies.



- Such an arrangement of myofilaments produces blebs of cell membrane when the muscle contracts, and these blebs disappear when the muscle relaxes (Fig. 9.12).

#### *Thick Filament*

- It is composed of myosin protein.
- Thick filaments are not always present in the sarcoplasm. The myosin molecules aggregate into thick filaments in response to the stimulus, before the contraction begins.
- Each thick filament is surrounded by 12–15 thin filaments.

#### *Thin Filament*

- It is composed of actin and tropomyosin. There is no troponin.

### **CONTRACTION OF SMOOTH MUSCLES**

- As in the striated muscle, in response to the electrical stimulus, there is influx of calcium into the sarcoplasm from the sarcoplasmic reticulum.
- In the smooth muscle, the calcium ion is complexed to calmodulin (a calcium-binding protein).
- The calcium calmodulin complex activates myosin light-chain kinase. This enzyme phosphorylates the myosin, and allows it to bind to actin.
- Sliding of myofilaments occurs, as in the skeletal muscle, to produce contraction. Spread of the electrical stimulus is facilitated by the presence of gap junctions.

### **OTHER CONTRACTILE CELLS**

- These are not muscle cells, but they have the ability to contract. Myoepithelial cells, myofibroblasts and pericytes are the contractile cells.
- These cells have myofilaments composed of contractile proteins.

#### **MYOEPITHELIAL CELLS**

- Myoepithelial cells are present in exocrine glands like salivary glands.
- These are spindle-shaped cells, located within the basal lamina of the secretory acini and the ducts of the glands. They are illustrated in Figure 14.1, page 197.
- Contractions of these cells propel the secretions from the acini and the duct.

#### **MYOFIBROBLASTS**

- They resemble fibroblasts.
- These cells help in wound healing by contracting the edges of the wound.

#### **PERICYTES**

- Pericytes are wrapped around the capillaries outside the basement membrane. They are illustrated in Figure 10.4, page 130.
- Since they have contractile proteins, they may function as contractile cells and alter the capillary blood flow.
- After injury, these cells have the capacity to differentiate into fibroblasts and take part in repair process.



## CLINICAL CORRELATES

### Hypertrophy

- An increase in the diameter of individual muscle fibres is called hypertrophy. All types of muscles undergo hypertrophy in response to stress. The muscles undergo hypertrophy due to exercise in a bodybuilder, and cardiac muscles undergo hypertrophy due to increase in blood pressure.

### Hyperplasia

- An increase in the number of muscle fibres is called hyperplasia. Only the smooth muscle undergoes hyperplasia, and in pregnancy the uterus enlarges due to hyperplasia and hypertrophy of smooth muscles present in its wall.

### Asthma

- Constriction of airways in asthma is due to overactivity of smooth muscles present in the airways.

## KEYPOINTS

### Types of Muscles

These are skeletal, cardiac and smooth muscles.

Features	Skeletal muscle (Fig. 9.1; PMG 9.1)	Cardiac muscle (Fig. 9.10; PMG 9.2)	Smooth muscle (Fig. 9.13; PMG 9.3)
Muscle fibres	Cylindrical and unbranched	Cylindrical and branched	Spindle shaped and unbranched
Nuclei	Multiple, flat and at the periphery	One (occasionally two) oval nucleus in the centre	One oval nucleus in the centre
Striations	Present	Present	No striations
T tubules and sarcoplasmic reticulum	Form triads at the A-I junction	Form dyads at Z discs	None
Gap junctions	Absent	Present	Present
Regeneration after injury	Yes	No	Yes

## SELF-ASSESSMENT

1. How are muscles classified? Compare the microscopic features of skeletal, cardiac and smooth muscles.
2. What produces striations in the skeletal muscles?
3. What is a sarcomere? Describe its structure.
4. What do you understand by thin and thick filaments of the skeletal muscle?
5. What is an intercalated disc?
6. What are the differences between the skeletal and cardiac muscles?
7. What are dense bodies?
8. What are the differences between the smooth and skeletal muscles?

# Circulatory System

The circulatory system transports various substances, such as nutrients, gases and hormones, to various organs and tissues of the body and collects metabolic wastes from them.

## COMPONENTS OF THE CIRCULATORY SYSTEM

- The circulatory system is subdivided into two major components:
  - (a) The blood vascular system
  - (b) The lymph vascular system
- The components of the blood vascular system are blood vessels and heart, while the components of the lymph vascular system are lymphatic capillaries and ducts.
- Small vessels in the tissues and organs constitute microcirculation, which includes arterioles, venules, capillaries and lymphatic capillaries.

## BLOOD VESSELS

- Blood vessels are classified into two groups: arterial and venous systems.
- The arterial system transports blood away from the heart to the various organs and tissues of the body. It includes arteries, arterioles and capillaries.
- The venous system returns blood to the heart from the various organs and tissues of the body. It includes venules and veins.

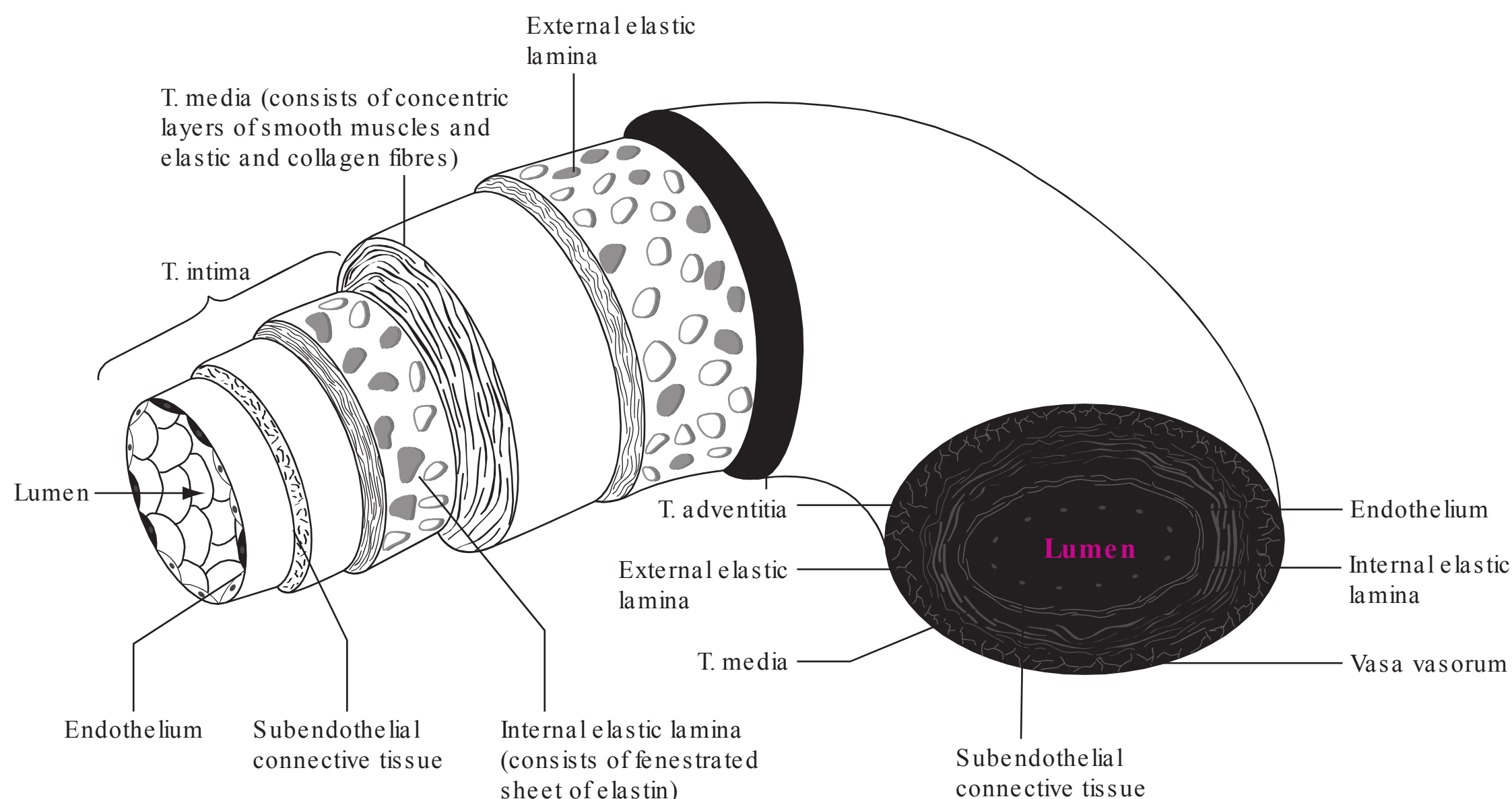
## BASIC STRUCTURE OF BLOOD VESSELS

- Based on their diameters, blood vessels, both arteries and veins, can be large, medium or small in type.
- Histologically, the wall of the blood vessels is composed of three coats or tunics: tunica (T) intima, tunica media and tunica adventitia (from inside to outside) (Fig. 10.1).
- The thickness of these walls, chiefly of the media and adventitia, varies depending on the type of the blood vessel.

### Tunica Intima

- Tunica intima is the innermost layer.
- It consists of endothelium (facing the lumen of the blood vessel), subendothelial connective tissue and internal elastic lamina (Fig. 10.1).





**Figure 10.1** Schematic diagram of an artery. At one end (the end showing the lumen with the arrow) it shows the three-dimensional organisation of the various layers of the artery, and at the other end transverse section of the artery can be seen.

- The endothelium consists of simple squamous epithelium; the endothelial cells (squamous cells) rest on a basal lamina.
- Underneath this endothelium, there is subendothelial connective tissue, which consists of loose connective tissue.
- Internal elastic lamina separates tunica intima from tunica media. It consists of a fenestrated sheet of elastin (Fig. 10.1). Through these fenestrations, nutrients reach the outer layer of the blood vessels from the blood present in the lumen of the blood vessel.

### Endothelium

- Endothelial cells are held together by occluding junctions.
- The cytoplasm of these cells shows numerous pinocytotic vesicles. Pinocytotic vesicles help in transport of materials from blood to the underlying tissue.
- Endothelial cells secrete several substances which are involved in diapedesis (the process by which leucocytes pass through endothelial cells), clotting of blood and maintenance of tone of smooth muscles of the blood vessels.
- Some of the substances secreted by endothelial cells are as follows:
  - (a) Nitric oxide: It causes relaxation of vascular smooth muscles, which results in vasodilation.
  - (b) Prostacyclin: It causes vasodilation and inhibits platelet adhesion.
  - (c) Thromboplastin and von Willebrand factor: Both these factors are involved in blood coagulation.

### Tunica Media

- Tunica media is the middle layer (Fig. 10.1). It consists of concentric layers of smooth muscles and elastic and collagen fibres. There are several layers of perforated sheets of elastin. In between these sheets, there are smooth muscles and collagen fibres.

- Tunica media is thicker in arteries than in veins of similar size. In arteries, it has relatively more smooth muscle and elastic fibres than in a vein of comparable size.
- Contraction and relaxation of the smooth muscles is under the control of the autonomic nervous system. These smooth muscles communicate with each other through gap junctions.
- In the arteries, the media is separated from adventitia by external elastic lamina. External elastic lamina is similar to internal elastic lamina, except that the former is thinner than the latter.

### Tunica Adventitia

- Tunica adventitia is the outermost layer (Fig. 10.1).
- It consists of connective tissue, chiefly collagen fibres. It also contains some elastic fibres.
- The connective tissue of tunica adventitia is continuous with the connective tissue of the organ in which the vessel is located; hence, there is no distinct outer limit to the tunica adventitia.

### NOURISHMENT OF BLOOD VESSELS

- In small- and medium-sized blood vessels, all the layers get oxygen and nourishment by diffusion from the blood present within the lumen of the blood vessel.
- In large-sized blood vessels, the oxygen and nourishment cannot reach the outer parts of the media and adventitia. There are small blood vessels within these layers which nourish these layers. These small blood vessels are called vasa vasorum (Figs 10.1–10.3).

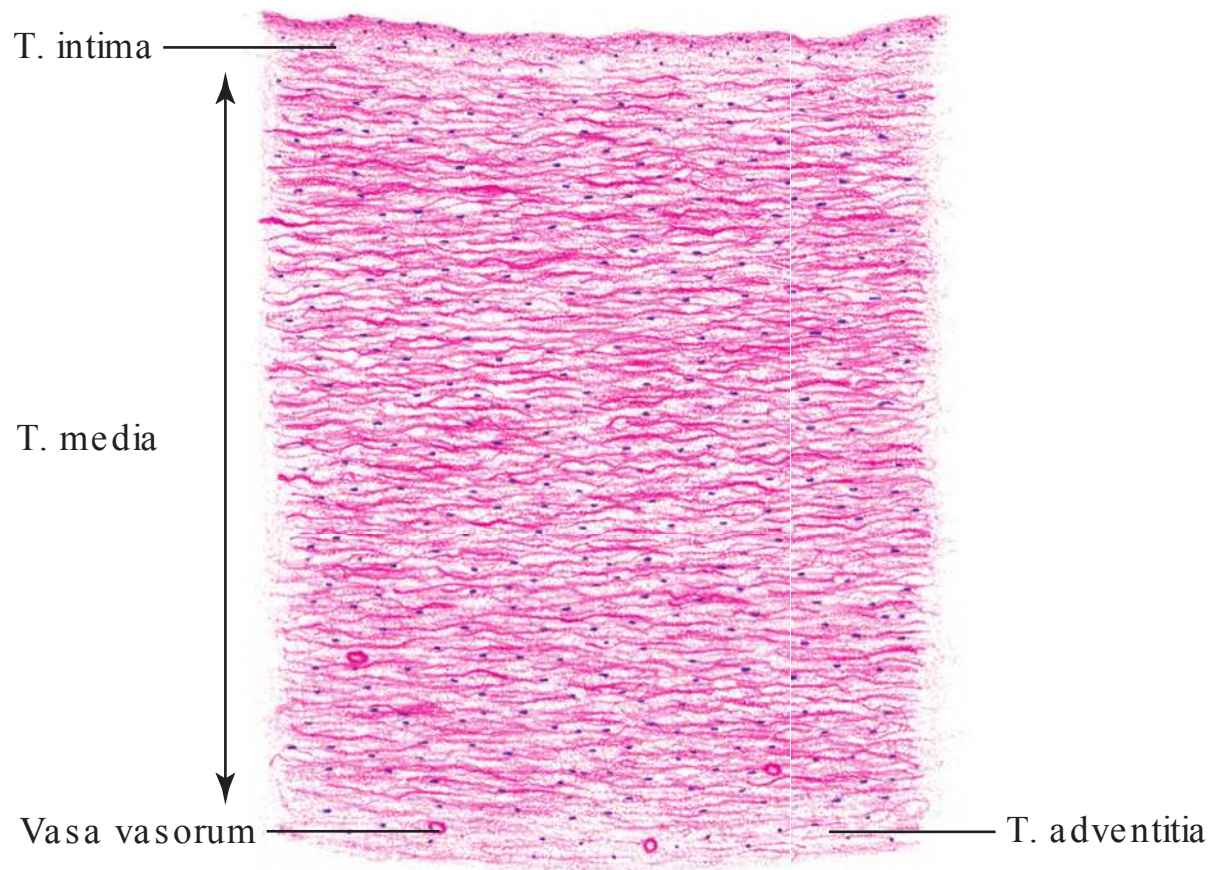
## ARTERIES

- Arteries carry blood away from the heart to various tissues and organs.
- As mentioned previously, tunica media of an artery is relatively more thick, having more smooth muscle and elastic fibres than a vein of comparable size.
- The arterial system consists of elastic and muscular arteries, arterioles and capillaries.
- Large arteries are elastic arteries, and tunica media of these arteries has more elastic fibres and less smooth muscles as compared to muscular arteries.
- Medium-sized arteries are muscular arteries with diameters of 0.5–10 mm. Tunica media of these arteries has more smooth muscles and less elastic fibres.

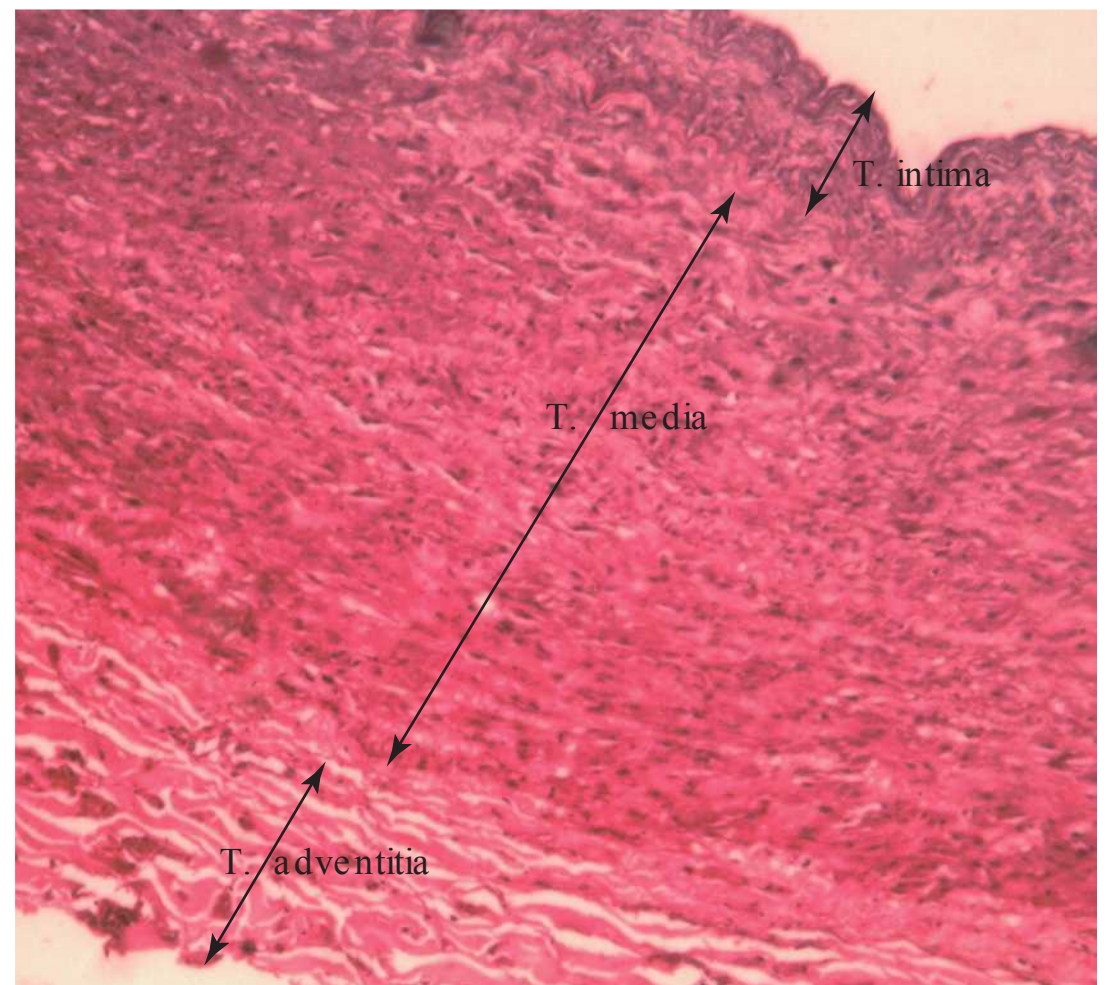
### ELASTIC ARTERY (Fig. 10.2; PMG 10.1)

- Elastic arteries are also called large arteries or conducting arteries.
- Their intimal layer consists of endothelium, subendothelial connective tissue and internal elastic lamina. However, the internal elastic lamina cannot be distinguished due to the presence of a large component of elastic tissue.
- Tunica media is thick, having several layers of perforated sheets of elastin. Elastic fibres can be demonstrated in the elastic Van Gieson stained sections. Collagen fibres and smooth muscles are present in between the sheets of elastic fibres.
- Elastic fibres facilitate distension of the vessel wall. During ventricular systole, blood is expelled into elastic arteries, and these arteries expand due to the presence of this large component of elastic tissue. During ventricular diastole, these arteries recoil and force the blood forwards. These changes in the elastic arteries help in reducing the changes in blood pressure when the heart contracts, and thus help in maintaining the arterial blood pressure.
- Tunica adventitia is relatively thin (Fig. 10.2).
- Examples: Aorta and brachiocephalic, common carotid and subclavian arteries.





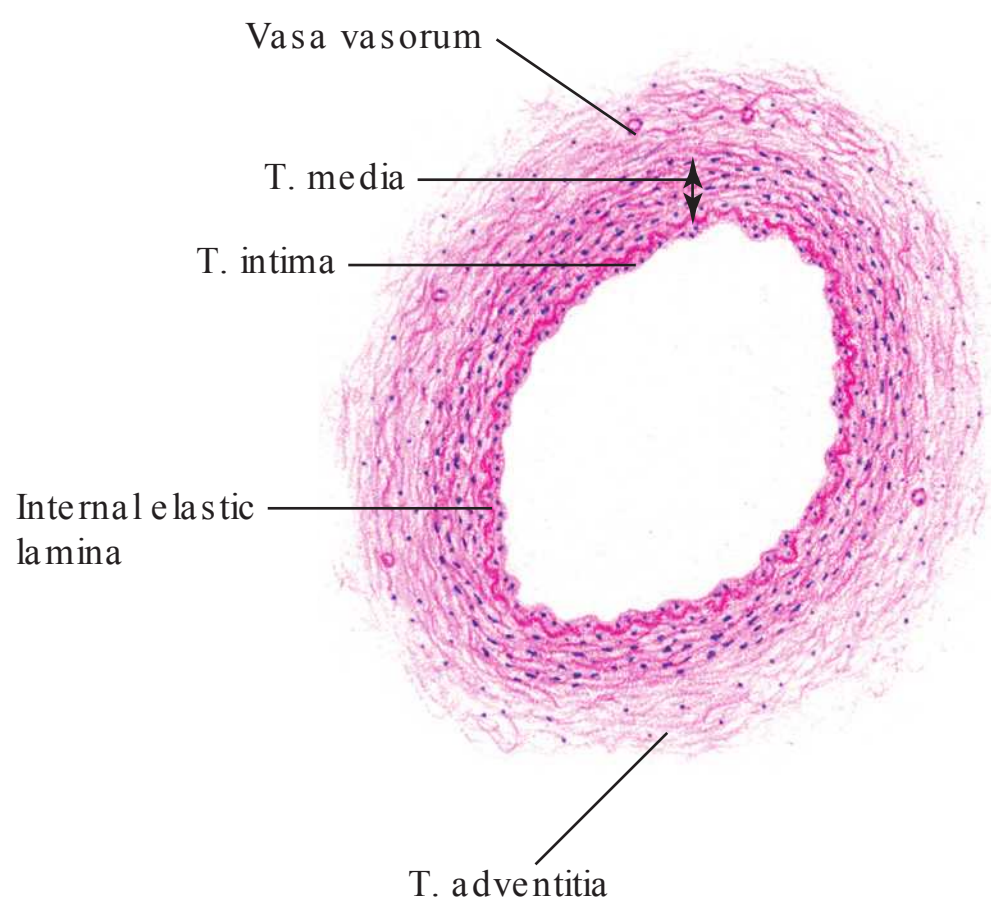
**Figure 10.2** Transverse section of an elastic (large) artery in low magnification. Note that T. media has relatively more elastic fibres (H&E pencil drawing).



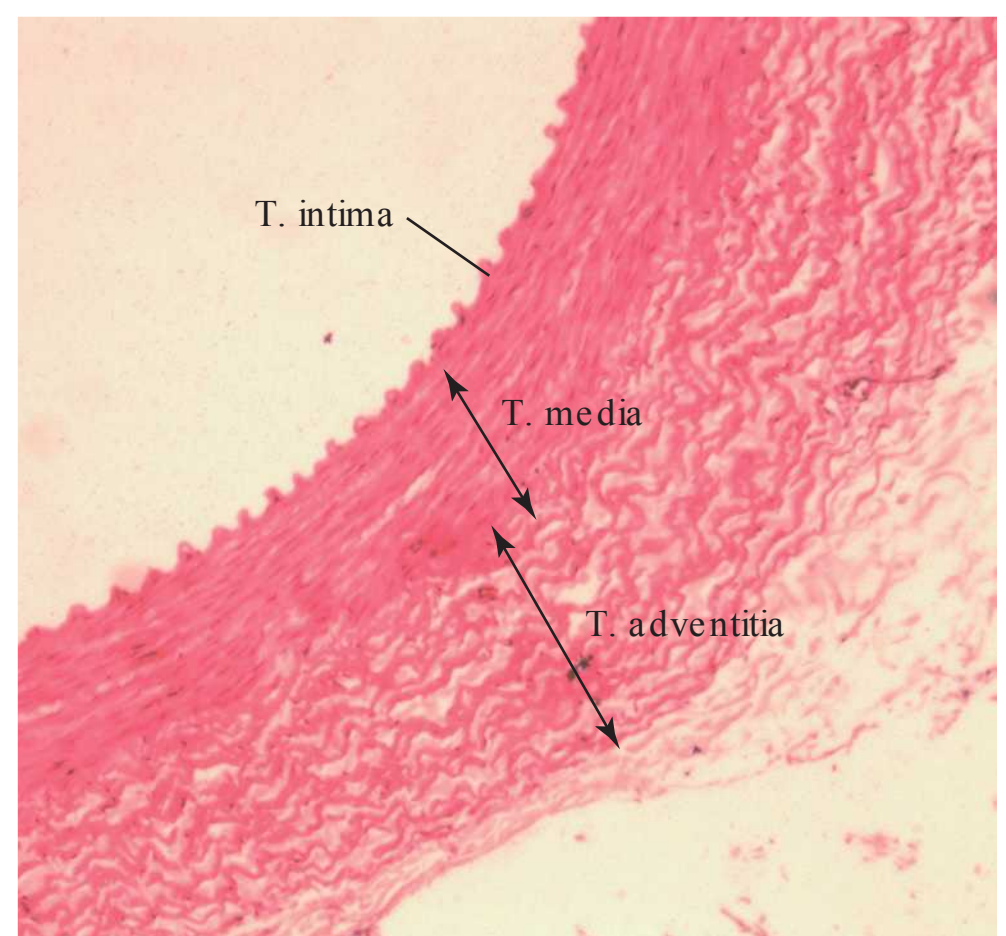
**PMG 10.1** Transverse section of large artery (H&E stain, X10).

### MUSCULAR ARTERY (Fig. 10.3; PMG 10.2)

- Muscular arteries are also called medium-sized arteries or distributing arteries as they arise from the large elastic arteries and distribute blood to various tissues and organs.
- T. intima is thin; however, a well-distinguished internal elastic lamina is seen (Fig. 10.3).
- Tunica media is thick and has relatively more layers of smooth muscles (Fig. 10.3).



**Figure 10.3** Transverse section of a muscular (medium) artery in low magnification. Note that T. media has relatively more smooth muscles and a well-developed internal elastic lamina (H&E pencil drawing).



**PMG 10.2** Transverse section of medium-sized artery (H&E stain, X10).



- T. adventitia is also thin.
- Examples: Arteries of the limbs, brachial artery and femoral artery.

### **ARTERIOLE** (see Fig. 10.8)

- Arterioles arise from muscular arteries; these are thin-walled, small arteries with diameters of 20–500  $\mu\text{m}$ .
- In arterioles, tunica intima is thin and subendothelial connective tissue is absent. Internal elastic lamina is thin and it gradually disappears.
- Tunica media consists of two or three layers of concentrically arranged smooth muscles. As arterioles branch, layers of smooth muscle cells progressively decrease.
- Tunica adventitia is very thin.
- Arterioles are the main regulators of peripheral vascular resistance. Contraction and relaxation of the smooth muscles present in the walls of the arterioles can alter the peripheral vascular resistance (or blood pressure) and the blood flow.

### **Metarterioles** (see Fig. 10.8)

- Metarterioles are the smallest arterioles.
- They have discontinuous layers of smooth muscle.
- They terminate into capillaries.
- In the terminal portion of the metarterioles, just before the beginning of the capillaries, the smooth muscles in the walls of the metarterioles form precapillary sphincters. These sphincters regulate the flow of blood to the capillaries.

## **CAPILLARIES**

- Capillaries are the smallest blood vessels.
- They are thin-walled blood vessels which form a network (see Figs 10.8 and 10.9). One end of the network is continuous with the smallest arterioles and another end with the smallest venules.
- Capillaries are the site for exchange of gases, nutrients and metabolic wastes between the tissue and blood as these substances can pass through the thin walls of the capillaries.
- The capillary wall is formed by a single layer of endothelial cells and basal lamina.
- Pericytes, the contractile cells wrapped around the capillaries outside the basal lamina, can be seen occasionally.
- According to the appearance of the wall of the capillaries under electron microscope, capillaries are of three types: continuous, fenestrated and sinusoidal.
- Continuous and fenestrated capillaries have diameters of 6–10  $\mu\text{m}$ . Sinusoidal capillaries are larger than continuous and fenestrated capillaries; they have diameters of 30–40  $\mu\text{m}$ .

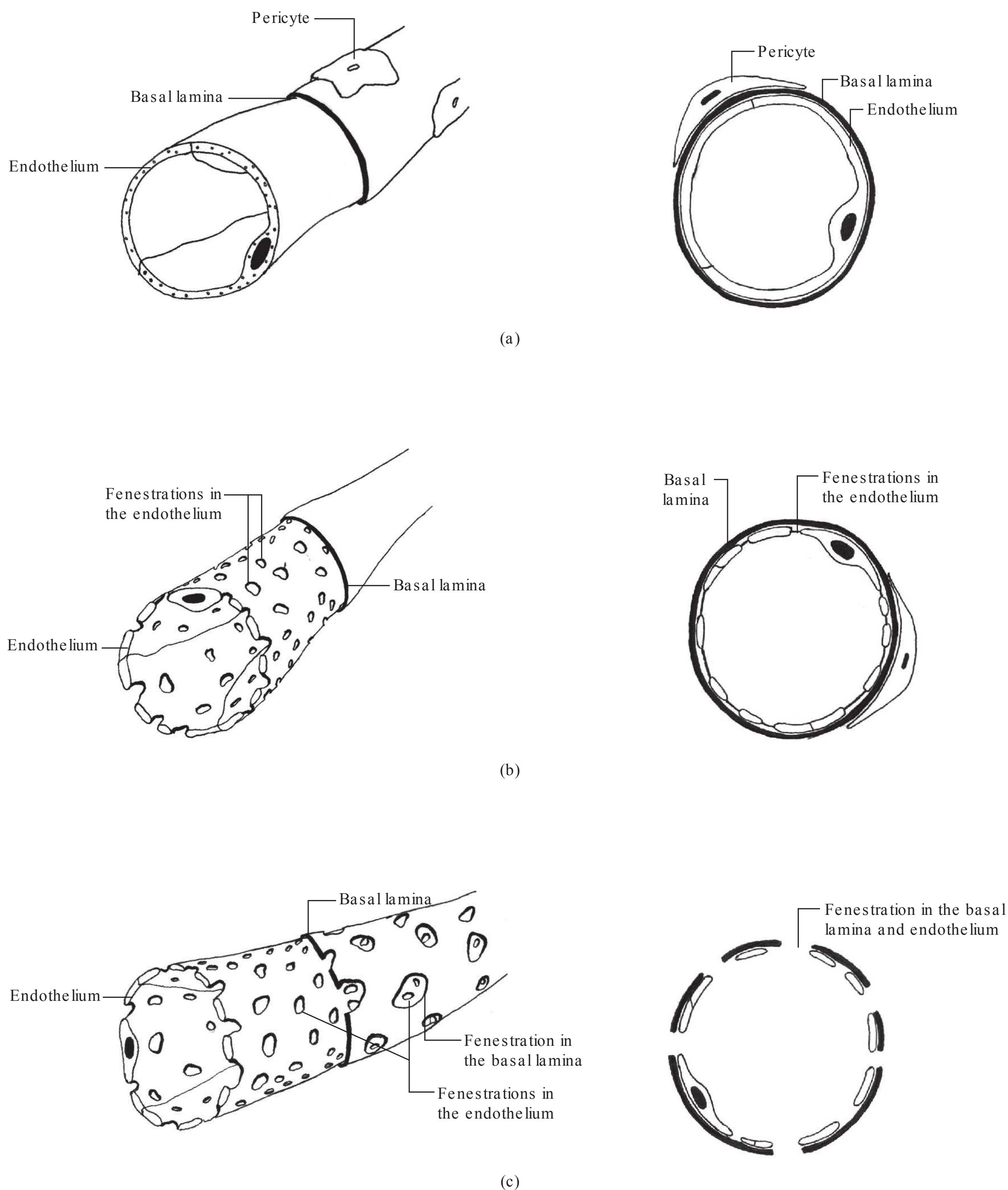
### **CONTINUOUS CAPILLARIES** (Fig. 10.4a)

- Endothelial cells and basal lamina are continuous without any fenestrations.
- Such capillaries are present in muscles, nervous tissues, etc.

### **FENESTRATED CAPILLARIES** (Fig. 10.4b)

- Endothelial cells have fenestrations, 70–90 nm in diameter, through which interstitial fluid or the components of blood can pass.
- Fenestrations in endothelial cells are covered by a thin membrane known as diaphragm. Not much is known about its nature and function.





**Figure 10.4** Types of capillaries: (a) continuous—endothelial cells and basal lamina are continuous without any fenestrations, (b) fenestrated—endothelial cells are fenestrated and basal lamina is continuous and (c) sinusoidal—both endothelial cells and basal lamina are fenestrated. Left: 3-D view; right: transverse section.

- Basal lamina is continuous.
- These capillaries are present in endocrine glands, small intestine and glomeruli of kidneys.
- In glomeruli of kidneys, fenestrations in capillaries lack diaphragm.

### SINUSOIDAL CAPILLARIES (Fig. 10.4c)

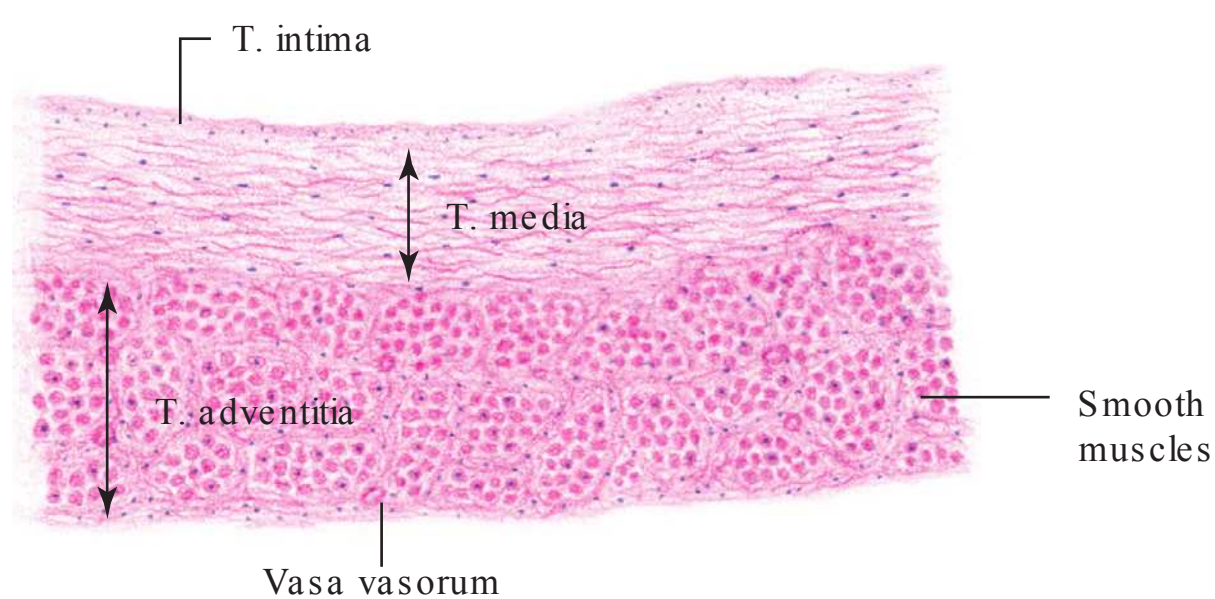
- Sinusoidal capillaries are large capillaries with irregular shape.
- Endothelial cells are fenestrated. Basal lamina is discontinuous.
- These capillaries are present in large numbers in red bone marrow, liver and spleen.

## VEINS

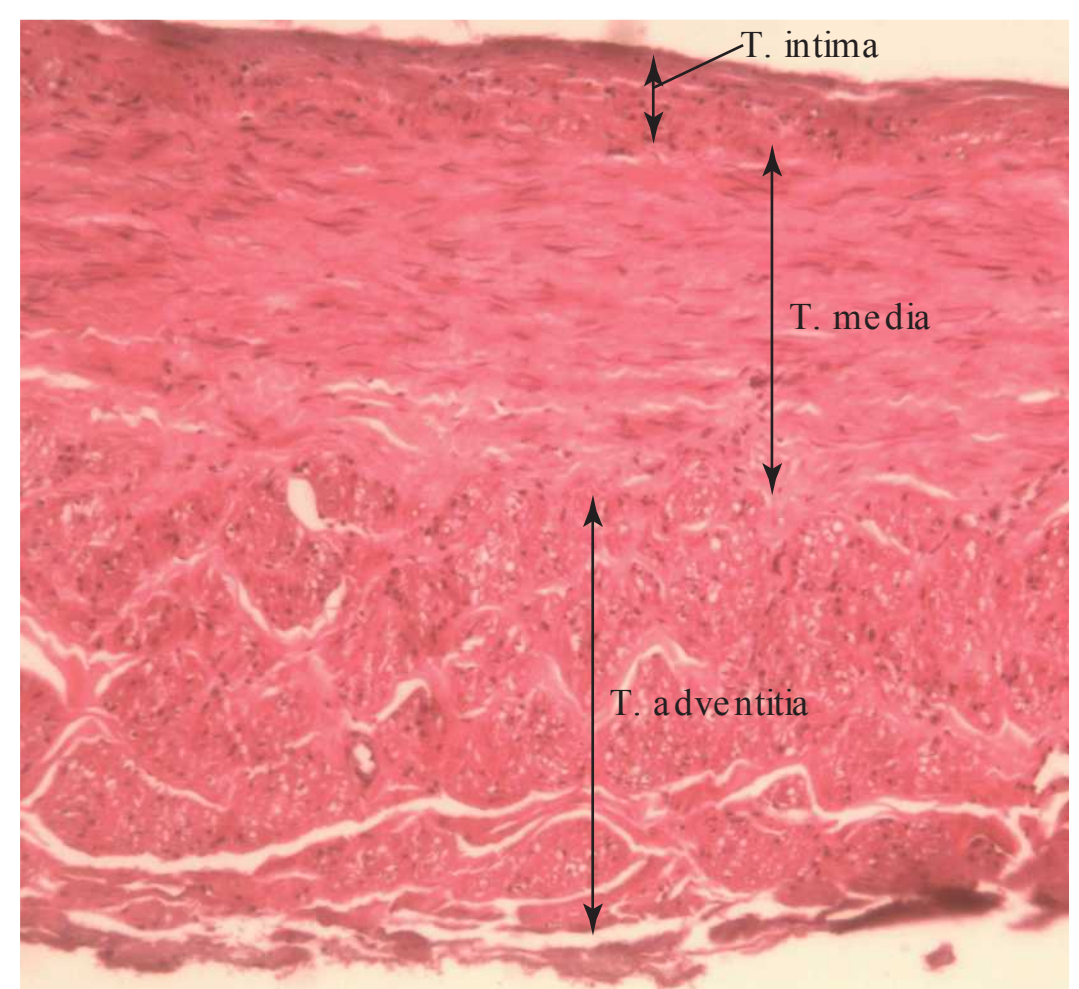
- Veins carry blood from the capillaries to the heart. The venous system includes venules and small-, medium- and large-sized veins. The postcapillary venules begin at the venous end of the capillary plexus and drain into large muscular venules. The large muscular venules drain into small-sized veins.
- The wall of a vein is thinner and has relatively less smooth muscle and elastic fibres than an artery of comparable size. Unlike arteries, in which tunica media is thick and most prominent, in veins tunica adventitia is thick and most prominent.
- The lumen of veins is collapsed.
- In general, veins have valves which help to maintain unidirectional flow of blood.
- Contraction of skeletal muscles surrounding the veins in the limbs and negative intrathoracic pressure created during inspiration help in venous circulation of the blood.

### LARGE-SIZED VEIN (Fig. 10.5; PMG 10.3)

- Veins with a diameter of 1 cm or more are large-sized veins.
- Internal elastic lamina is poorly defined (Fig. 10.5).



**Figure 10.5** Transverse section of a large vein in low magnification (H&E pencil drawing).



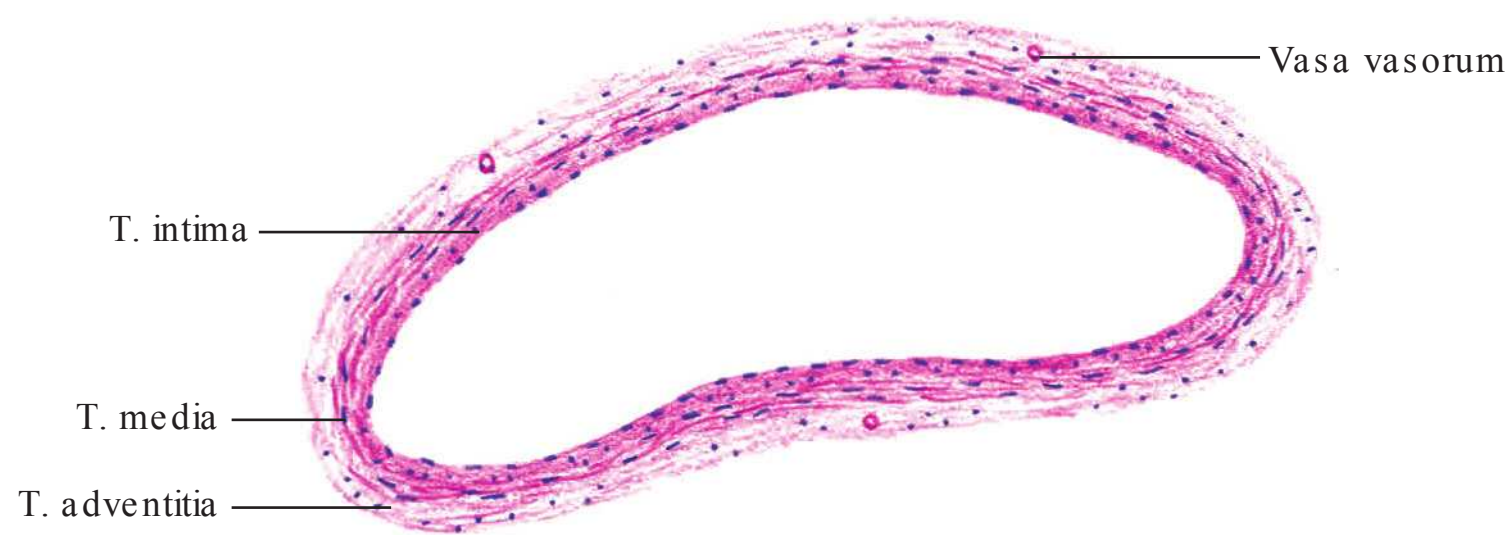
**PMG 10.3** Transverse section of large vein (H&E stain, X10).



- Tunica media is thin and has less smooth muscle.
- Tunica adventitia is well developed and is the thickest layer. Bundles of longitudinally arranged smooth muscles are present in tunica adventitia.
- Examples: Superior vena cava and inferior vena cava.

#### **MEDIUM-SIZED VEIN (Fig. 10.6; PMG 10.4)**

- Medium-sized veins have a diameter of 1–10 mm.
- All three layers are thinner than the corresponding layers in a large vein.
- Internal elastic lamina is poorly defined.
- Tunica media is less muscular (Fig. 10.6).
- Tunica adventitia is well developed.
- Examples: Femoral vein and superior mesenteric vein.



**Figure 10.6** Transverse section of a medium-sized vein in low magnification (H&E pencil drawing).



**PMG 10.4** Transverse section of medium-sized vein (H&E stain, X10).

### SMALL-SIZED VEIN

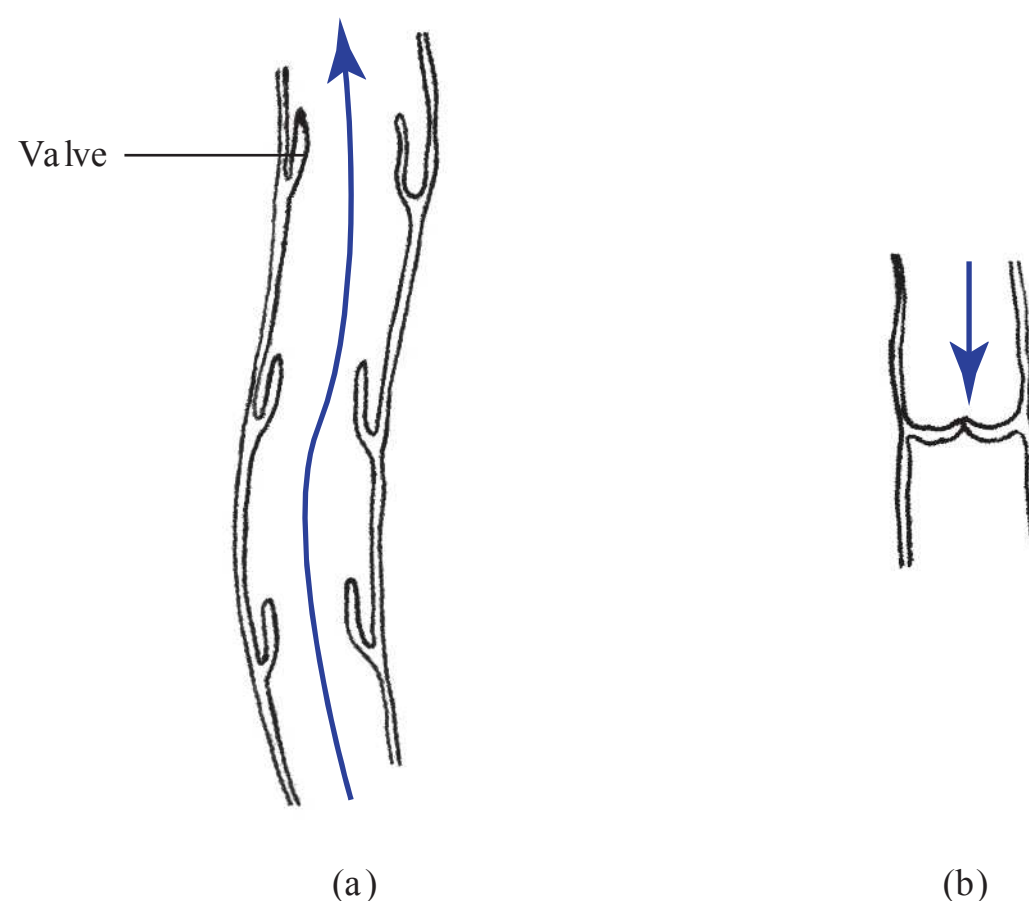
- Small-sized veins have a diameter of 0.1–1 mm.
- They are similar to medium-sized veins. Their wall is thin and diameter is small.

### VENULES (see Fig. 10.8)

- Capillaries drain into postcapillary venules, and postcapillary venules drain into large muscular venules. The diameter of postcapillary venules is 10–40  $\mu\text{m}$  and that of large muscular venules is 40–100  $\mu\text{m}$ .
- Venules are important sites for exchange of metabolites.
- The smallest venules have tunica intima and adventitia. As the size of venules increases, smooth muscles appear and form tunica media.

### VENOUS VALVES

- Venous valves are folds of tunica intima projecting into the lumen of the vein as flaps.
- Each valve has two flaps. It consists of fibroelastic connective tissue covered with endothelium.
- The free margins of the flaps are directed towards the blood flow (Fig. 10.7a). When blood flows towards the heart, the folds of the valves move towards the vessel wall (Fig. 10.7a). When backflow occurs, the folds of the valves are forced towards the lumen, occluding the lumen of the vessel and thus preventing the backflow of blood (Fig. 10.7b).

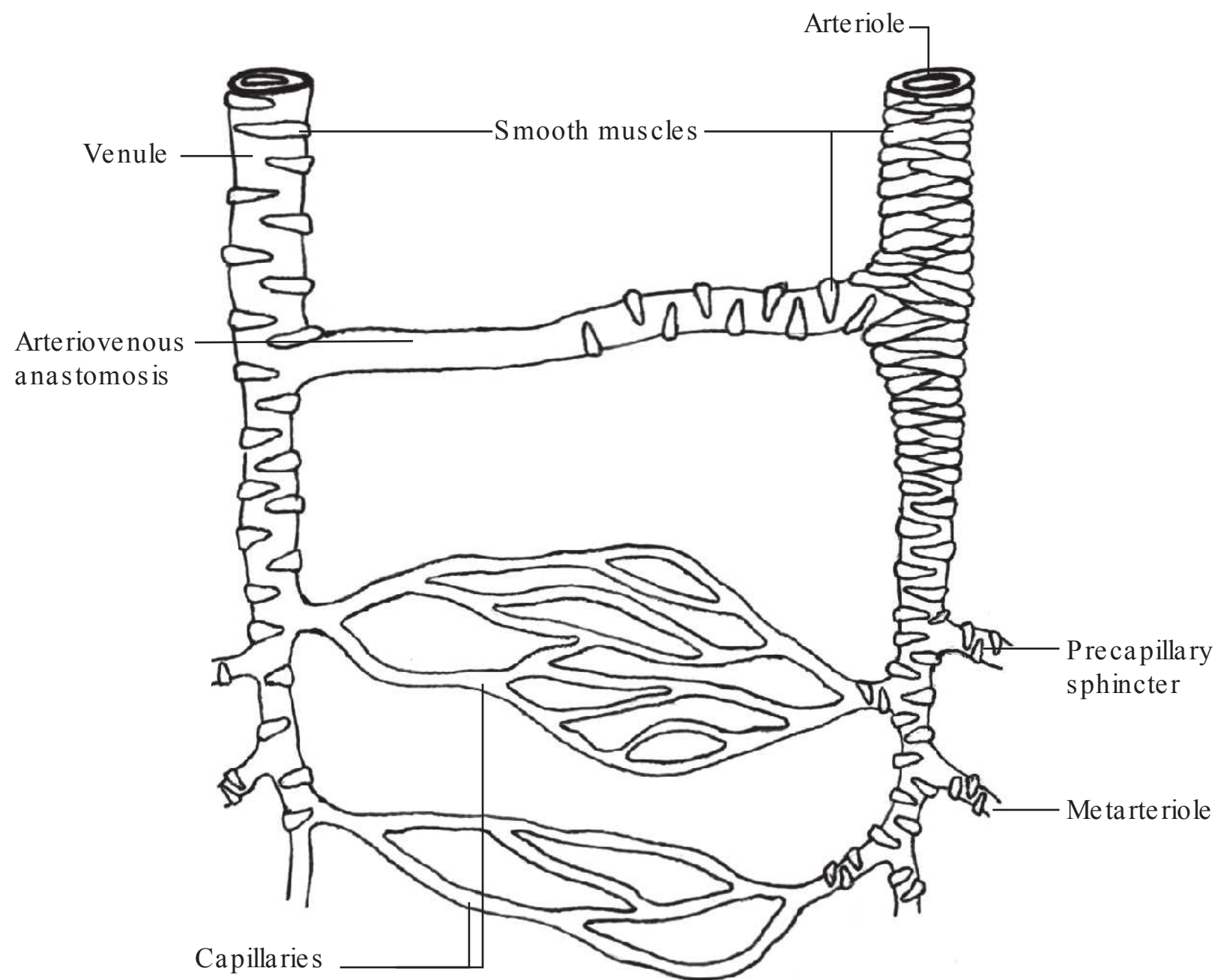


**Figure 10.7** Lower limb vein showing valves. (a) The flaps are turned towards the vessel wall as blood flows towards the heart. (b) Flaps occlude the lumen and prevent backflow. Blue arrows indicate the flow of blood.

### ARTERIOVENOUS ANASTOMOSIS

- These are small vessels which shunt blood directly from the arterioles to the venules, bypassing the capillary bed (Fig. 10.8).
- Tunica intima of these vessels consists of endothelium and connective tissue, and these vessels lack internal elastic lamina.





**Figure 10.8** Microcirculation showing arteriovenous anastomosis—metarterioles give rise to capillaries. Precapillary sphincters of metarterioles are also seen.

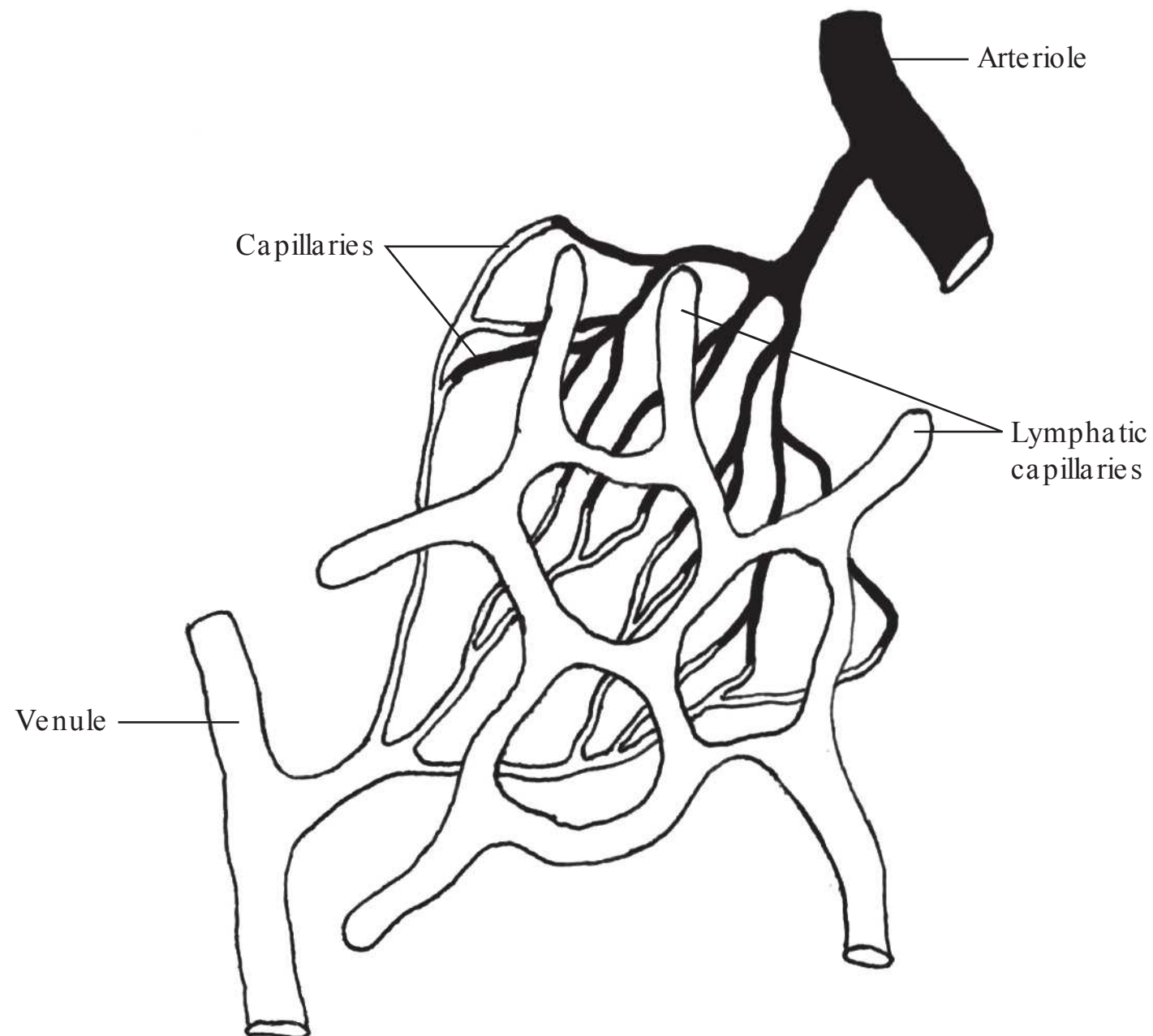
- Tunica media has abundant smooth muscles. Relaxation of these muscles opens up the anastomosis, and more blood enters the venules through them, bypassing the capillary bed. Contraction of the smooth muscles occludes the lumen and diverts the blood to the capillary bed.
- Arteriovenous anastomosis plays an important role in blood pressure regulation and thermoregulation by the skin.
- Skin of fingertips, toes, ear, nose and lips are the regions where arteriovenous anastomosis is commonly seen.

## LYMPHATIC VASCULAR SYSTEM

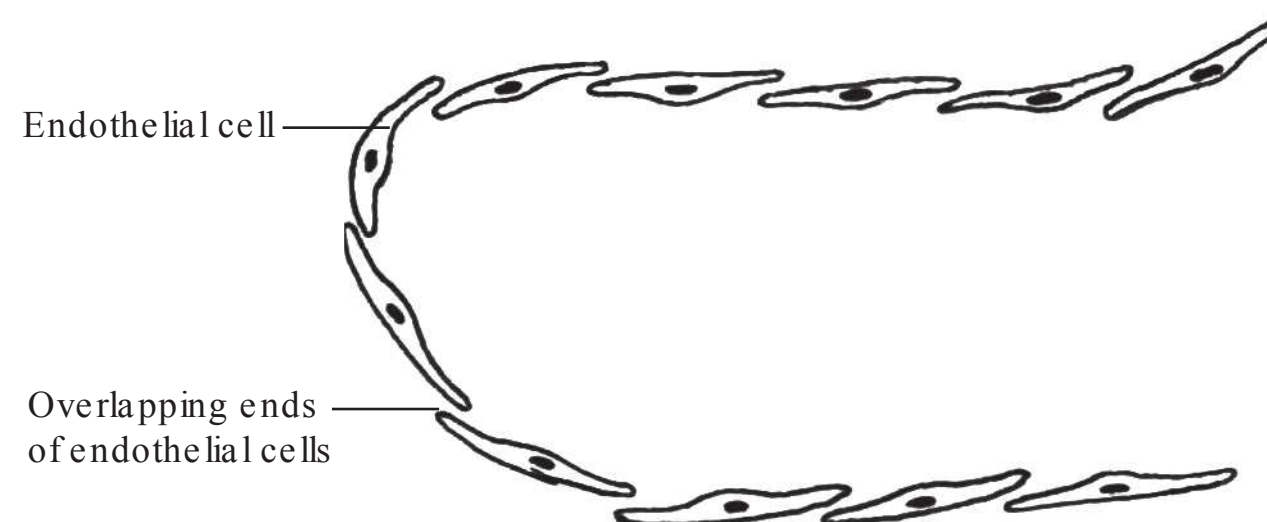
- In tissues, some plasma leaks out of the capillaries. A part of this is taken up at the venous end of the capillaries; the remaining fluid is called lymph, which is drained by lymphatic vessels. From lymphatic vessels, the lymph finally enters the systemic circulation through the thoracic duct (Fig. 11.2, page 139).
- Lymph nodes are present along the course of lymphatic ducts to filter the lymph.
- Lymphatics are present in all the tissues of the body except the central nervous system and bone marrow.
- Basic structure of these vessels is similar to blood vessels.

### LYMPHATIC CAPILLARIES

- Lymphatic capillaries begin in the tissue; these capillaries are closed at one end (Figs 10.9 and 10.10). They anastomose and form a network.
- They are lined by endothelial cells with a very thin basal lamina. The ends of the neighbouring endothelial cells overlap (Fig. 10.10).
- These capillaries unite to form thick-walled larger lymphatic ducts.



**Figure 10.9** Components of microcirculation—lymphatic capillaries are prominently seen here.



**Figure 10.10** Structure of a lymphatic capillary.

### LYMPHATIC DUCTS

- These vessels resemble veins of comparable size; however, their lumen and wall thickness is less than that of veins.
- They have valves which give them a beaded appearance.
- Tunica media has a few layers of smooth muscles.



## CLINICAL CORRELATES

### Atherosclerosis

- Atherosclerosis results from lesions in tunica intima called atheroma. Atheroma is accumulation of lipids which protrude into the lumen of the blood vessel and obstruct them. Atheroma may rupture and cause thrombus formation; it also weakens the tunica media. This can cause localised abnormal dilation of the blood vessels, known as aneurysm.

### Aortic Dissection

- Aortic dissection is a tear in the inner wall of the aorta that causes bleeding between the layers of the wall of the aorta and forces the layers apart. When it ruptures out, it causes massive haemorrhage and may become fatal.

## KEYPOINTS

### Blood Vessel Wall (Fig. 10.1)

Tunica intima	Tunica media	Tunica adventitia
<ul style="list-style-type: none"><li>Endothelium (simple squamous epithelium)</li><li>Subendothelial connective tissue (loose connective tissue)</li><li>Internal elastic lamina (fenestrated elastin sheets)</li></ul>	<ul style="list-style-type: none"><li>Concentrically arranged smooth muscles and collagen fibres</li><li>Fenestrated sheets of elastin</li><li>External elastic lamina</li></ul>	<ul style="list-style-type: none"><li>Collagen fibres</li><li>Elastic fibres</li><li>Vasa vasorum</li></ul>

### Comparative Features of Different Blood Vessels

In general, in histological preparation, veins tend to have collapsed lumen while arteries have round lumen.

<b>Large artery (Fig. 10.2; PMG 10.1)*</b> <ul style="list-style-type: none"><li>Tunica media is thick and muscular (look for the nuclei of smooth muscles)</li><li>Tunica adventitia is relatively thin</li></ul>	<b>Large vein (Fig. 10.5; PMG 10.3)</b> <ul style="list-style-type: none"><li>Tunica media is thin and less muscular</li><li>Tunica adventitia is well developed (notice the bundles of smooth muscles)</li></ul>
<b>Medium-sized artery (Fig. 10.3; PMG 10.2)</b> <ul style="list-style-type: none"><li>Well-defined internal elastic lamina</li><li>Tunica media is muscular (look for the nuclei of smooth muscles)</li></ul>	<b>Medium-sized vein (Fig. 10.6; PMG 10.4)</b> <ul style="list-style-type: none"><li>Poorly defined internal elastic lamina</li><li>Tunica media is less muscular</li></ul>

\*In large arteries, tunica media has more elastic fibres and less smooth muscles compared to the muscular artery.

## SELF-ASSESSMENT

- Describe the structure of a blood vessel.
- What is internal elastic lamina?
- Name the layers that comprise tunica intima.
- How does a large blood vessel get nutrition?
- Describe the different types of capillaries. Give examples for each.

# Lymphoid (Immune) System

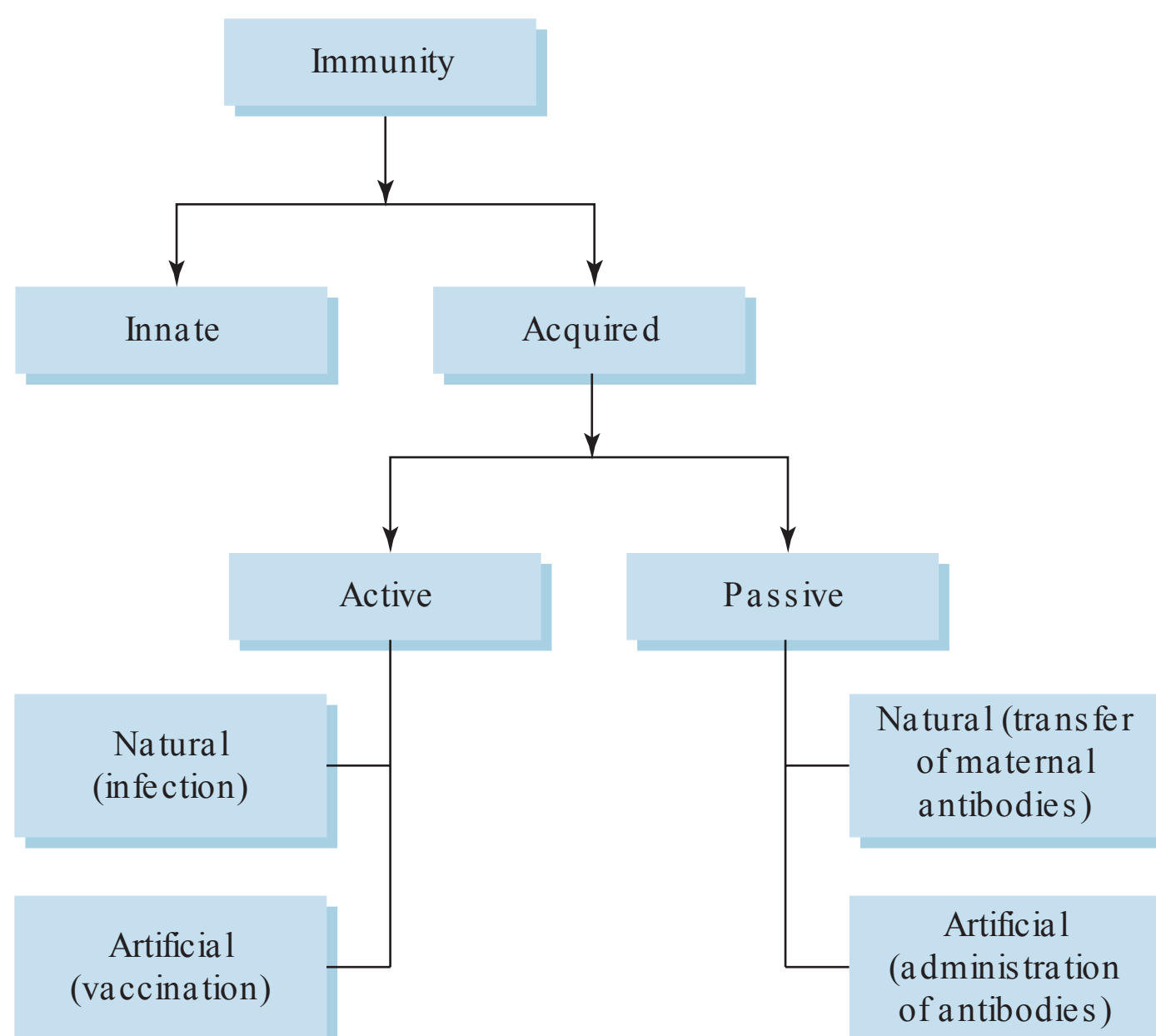
The lymphoid system provides protection against invasion of the body by microorganisms and foreign particles and against some types of endogenous cells which have become abnormal.

## IMMUNITY

There are two types of immunity: innate immunity and acquired (adaptive) immunity (Fig. 11.1).

### INNATE IMMUNITY

- Innate immunity is present from birth, and it provides non-specific defence. It prevents the entry, colonisation and spread of microorganisms inside the body. The main components of innate immunity are as follows:
  - Epithelial barrier: The intact epithelium of skin and the respiratory, gastrointestinal and genitourinary tracts protects the body from invasion by microorganisms.



**Figure 11.1** Types of immunity.



- (b) Inflammation: Tissue injury caused by microorganisms produces a non-specific response—the inflammation. Microorganisms are destroyed by the inflammatory cells that migrate from the blood into the damaged tissue.

## ACQUIRED IMMUNITY

- Acquired immunity is the immunity acquired during life and it is of two types (Fig. 11.1):
  - Active
  - Passive
- Active immunity is induced in an individual after antigen exposure; it involves active participation of immunocompetent cells, resulting in production of antibodies and immunologically active cells. Active immunity is long lasting. In passive immunity, there is no active participation of the immune system, and readymade antibodies are transferred to the individual.
- Both active immunity and passive immunity can be acquired artificially and naturally. Naturally acquired active immunity occurs when a person is infected by a microorganism. Artificially acquired active immunity is induced by a vaccine (which contains weakened or killed microorganisms or their toxins). Naturally acquired passive immunity occurs when maternal antibodies pass to the foetus. Artificially acquired passive immunity is acquired by the administration of antibodies.

## LYMPHOID SYSTEM

- The lymphoid system includes lymphatic vessels and lymphoid organs.
- Lymphatic vessels are closely associated with the blood vascular system, and they drain into the systemic circulation. Lymphatic vessels have already been discussed in Chapter 10.
- Large aggregations of lymphocytes form lymphoid organs (thymus, spleen, lymph nodes and tonsils). Smaller aggregations of lymphocytes are present in the walls of respiratory, gastrointestinal and genitourinary tracts; these constitute diffuse lymphoid tissue.

## CELLS OF LYMPHOID SYSTEM

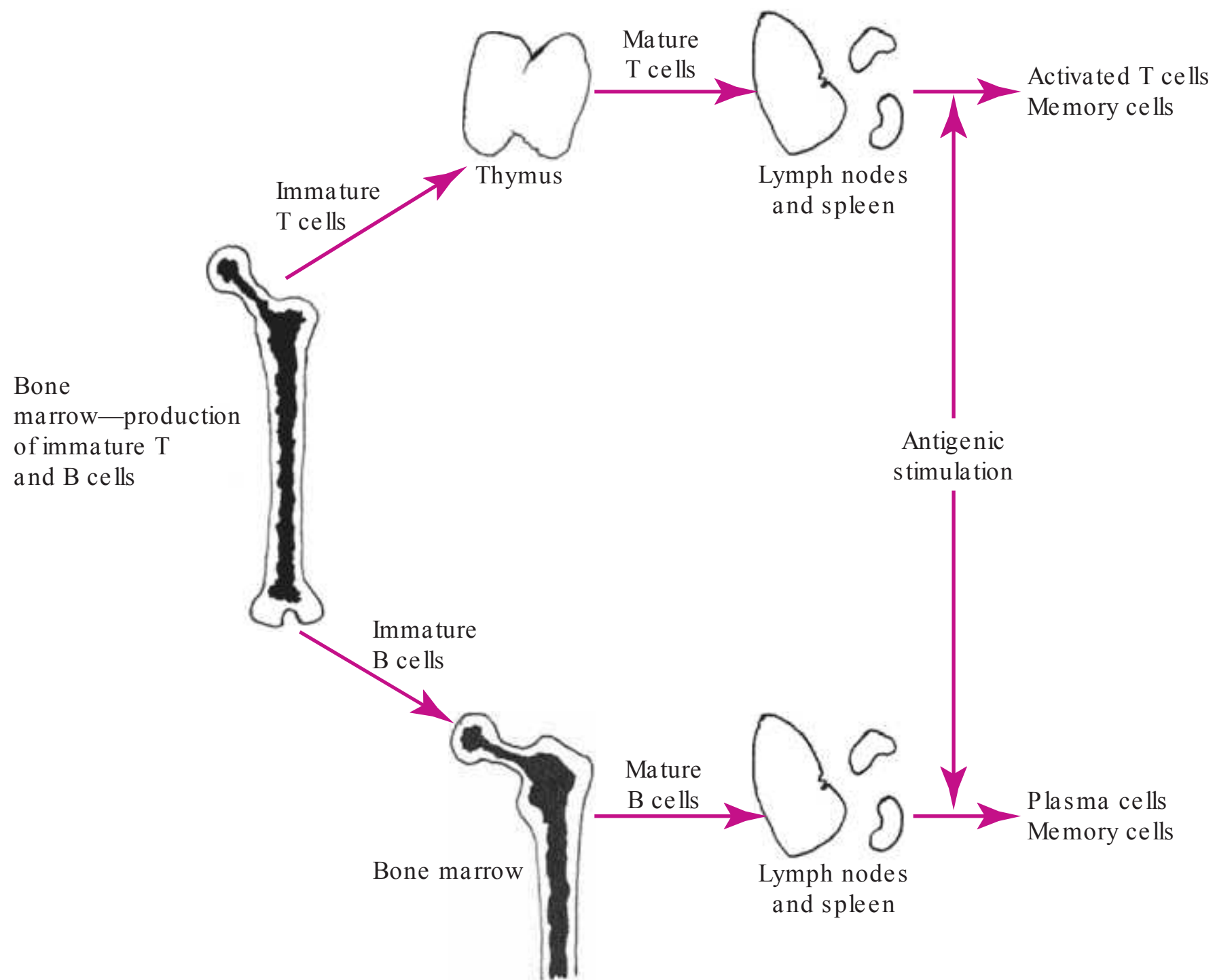
Lymphocytes are the principle cells of the immune system. Macrophages and reticular cells are also present.

### Lymphocytes

- All lymphocytes originate in the bone marrow. They are present in blood, lymph, tissue spaces and lymphoid tissues.
- There are three types of lymphocytes:
  - T lymphocytes
  - B lymphocytes
  - Natural killer (NK) cells

### *T Lymphocytes (T Cells)*

- T lymphocytes are responsible for cell-mediated immunity.
- They are produced in the bone marrow and mature in thymus (Fig. 11.2).
- These cells have receptors (T cell receptor [TCR]) to recognise the specific antigen. Based on the type of receptor present, T lymphocytes are classified into TCR1 and TCR2.
- These receptors recognise the antigen that is bound to the cell membrane proteins called major histocompatibility complex (MHC) molecules.



**Figure 11.2** Development of T and B cells.

- Recognition of the antigen bound to MHC molecule on a cell by T cells triggers the proliferation and differentiation of T cells into effector and memory T cells (Fig. 11.2).
  - (a) Effector T cells are of three subtypes: helper T cells, cytotoxic T cells and suppressor T cells.
    - (i) Helper T cells ( $T_H$  cells): These cells are the key regulators, and they assist almost all the other cells in immunological processes, including maturation of B cells into plasma cells, other subtypes of T lymphocytes and macrophages.
    - (ii) Cytotoxic T cells ( $T_C$  cells): They kill virally infected cells and tumour cells.
    - (iii) Suppressor T cells: These cells regulate the immune response by suppressing the helper T cells.
  - (b) Memory T cells: These cells persist for a long time after an infection has cleared. If a similar infection occurs again, these cells proliferate more rapidly and mount a faster and stronger immune response.

### *B Lymphocytes (B Cells)*

- B lymphocytes originate and mature in the bone marrow (Fig. 11.2).
- They are responsible for humoral immunity.
- These cells also have antigen-specific receptors on their surface; these receptors are immunoglobulin D (IgD) and M (IgM).
- Once activated, these cells differentiate into plasma cells, and a few cells become memory cells (Fig. 11.2).
- Plasma cells synthesise and secrete antibodies.
- Memory cells help in faster immune response during subsequent exposure to the same antigen (secondary response).



### *Natural Killer (NK) Cells*

- NK cells are another variety of lymphocytes. They are large lymphocytes with granular cytoplasm.
- They kill tumour cells and virus-infected cells.
- They destroy antibody-bound target cells, and this process is known as antibody-dependent cellular cytotoxicity (ADCC).

### **Macrophages**

- Macrophages are derived from monocytes.
- They function in humoral immunity as well as cellular immunity.
- These cells phagocytose the antigen, process them and present them to T cells.

### **Reticular Cells**

- In spleen, lymph node and tonsils, the structural framework is made up of a three-dimensional network of reticular fibres, which are produced by reticular cells. These networks of reticular fibres support lymphocytes, macrophages and other cells of the lymphoid tissue.
- The reticular cells of spleen, lymph node and tonsils are derived from mesoderm, whereas the reticular cells of thymus (described under 'Thymus') are endodermal in origin.

## **LYMPHOID NODULES (OR FOLLICLES)**

- Lymphocytes are organised into spherical masses in all the lymphoid organs except thymus. These spherical masses are referred to as lymphoid nodules. The lymphoid nodule is clearly delineated from the surrounding tissue.
- There are two types of lymphoid nodules: primary and secondary.

### **Primary Nodules**

- Primary nodules are uniform in appearance.
- They are present before birth.
- Secondary nodules become secondary nodules after antigen exposure.

### **Secondary Nodules**

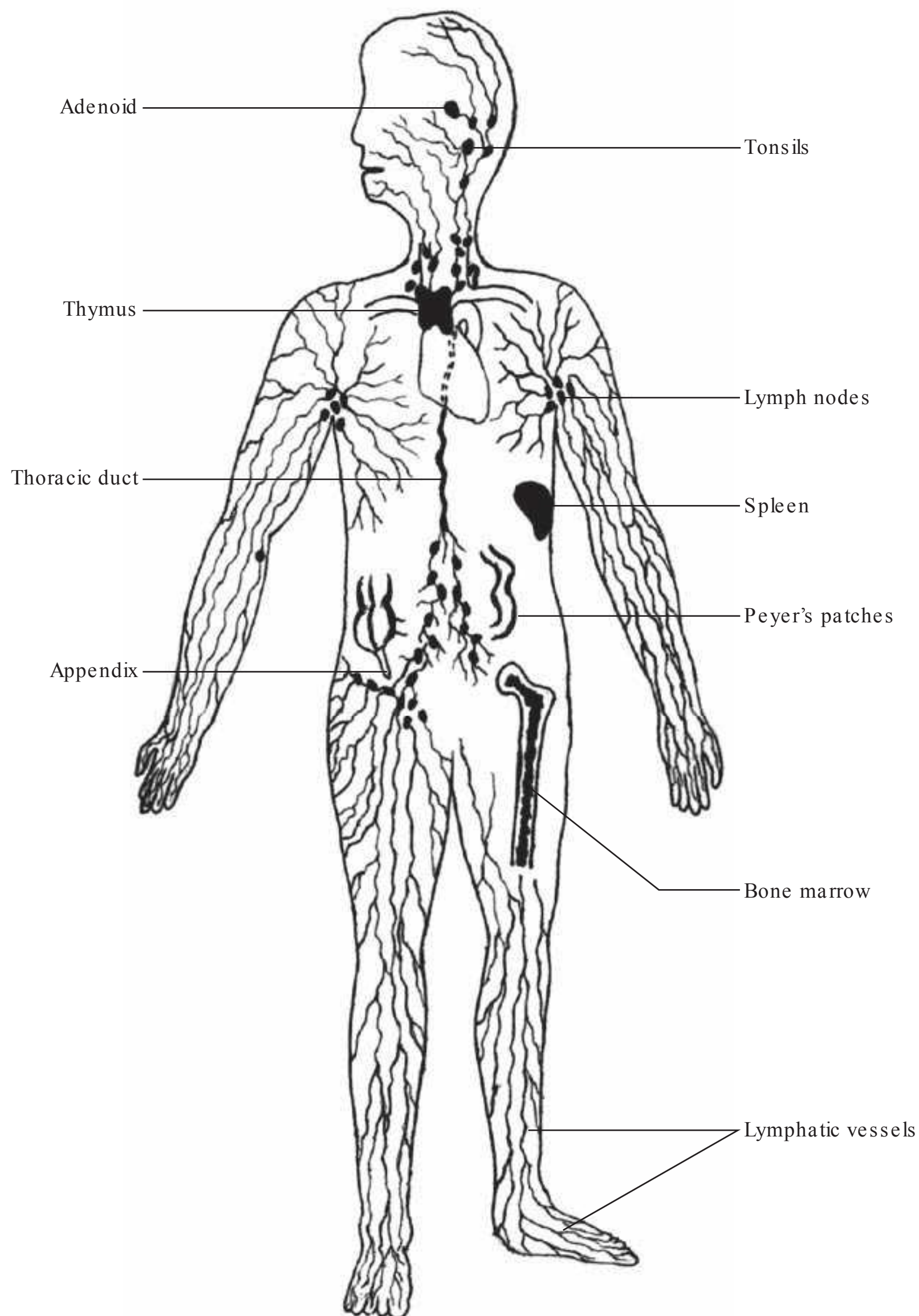
- Secondary nodules have a lightly stained central region, the germinal centre, surrounded by a peripheral dark region (see Fig. 11.5; PMG 11.3b).
- The germinal centre is the site for proliferation of B lymphocytes.
- Secondary nodules appear after birth following antigen exposure.

## **LYMPHOID ORGANS**

- As mentioned earlier, large lymphoid aggregates form lymphoid organs. Lymph node, thymus, spleen and bone marrow are the lymphoid organs.
- Lymph node, thymus and spleen are covered with a capsule of dense connective tissue. Extensions of the capsule entering the substance of the organ are known as trabeculae.
- On histological examination, a lymphoid organ may show two distinct zones: a central zone known as the medulla and a peripheral zone known as the cortex; the cortex surrounds the medulla. However, spleen does not show this kind of arrangement; instead it has white and red pulp (described in 'Spleen').
- Lymphoid organs are classified as follows:
  - (a) Primary (or central)
  - (b) Secondary (or peripheral)

### Primary Lymphoid Organs

- Thymus and bone marrow are the primary lymphoid organs (Fig. 11.3).
- Primary lymphoid organs are the sites of lymphocyte proliferation and maturation. T cell proliferation and maturation does not depend on antigenic stimulation.
- Both T and B lymphocytes are produced in the bone marrow. T lymphocytes leave the bone marrow and mature in the thymus. Lymphocytes produced in primary lymphoid organs migrate to secondary lymphoid organs.



**Figure 11.3** The lymphoid system. Primary and secondary lymphoid organs and lymphatic vessels are shown. Most of the lymphatic vessels eventually drain into the thoracic duct, which empties into the left subclavian vein.



## Secondary Lymphoid Organs

- Lymph node, spleen, Peyer's patches (in the small intestine), tonsils and appendix are the secondary lymphoid organs (Fig. 11.3). Numerous unencapsulated lymphoid follicles in the mucous membranes (mucosa-associated lymphoid tissue [MALT]), lining of the large intestines, in the upper airways and genital tract are also secondary lymphoid organs.
- Secondary lymphoid organs are the sites for interaction between mature lymphocytes and antigens to induce immune response.
- Lymphocytic proliferation in the secondary lymphoid organ is antigen dependent.

## Diffuse Lymphoid Tissue

- Mucosa of gastrointestinal, respiratory and genitourinary tracts are constantly exposed to various antigens, and these surfaces are protected by the presence of unencapsulated collection of lymphocytes. These lymphatic tissues constitute diffuse lymphoid tissue or MALT. In the gastrointestinal tract, they are called gut-associated lymphoid tissue (GALT), and those in the respiratory tract are called bronchus-associated lymphoid tissue (BALT).
- These lymphoid tissues are non-capsulated aggregations of lymphoid cells present underneath the epithelium in the lamina propria as lymphoid nodules.
- GALT includes Peyer's patches of ileum, adenoids (located in the roof of the pharynx), lingual tonsils (present in the posterior one-third of the tongue) and palatine tonsils. Tonsils are aggregates of lymphoid tissue present underneath the mucosa of the oral cavity and pharynx.

## THYMUS

- Thymus is a bilobed gland located in the superior mediastinum.
- In front, it is related to the manubrium and the muscles attached to it (sternothyroid and sternohyoid) and top four costal cartilages; behind, it is related to pericardium and the arch of aorta with three of its branches—brachiocephalic, left common carotid and left subclavian.
- The thymus gland undergoes atrophy after puberty.
- Functions: Precursor cells from the bone marrow get differentiated into T lymphocytes in thymus. Thymus produces and secretes thymic hormones which promote T-cell proliferation and maturation.

## MICROSCOPIC FEATURES

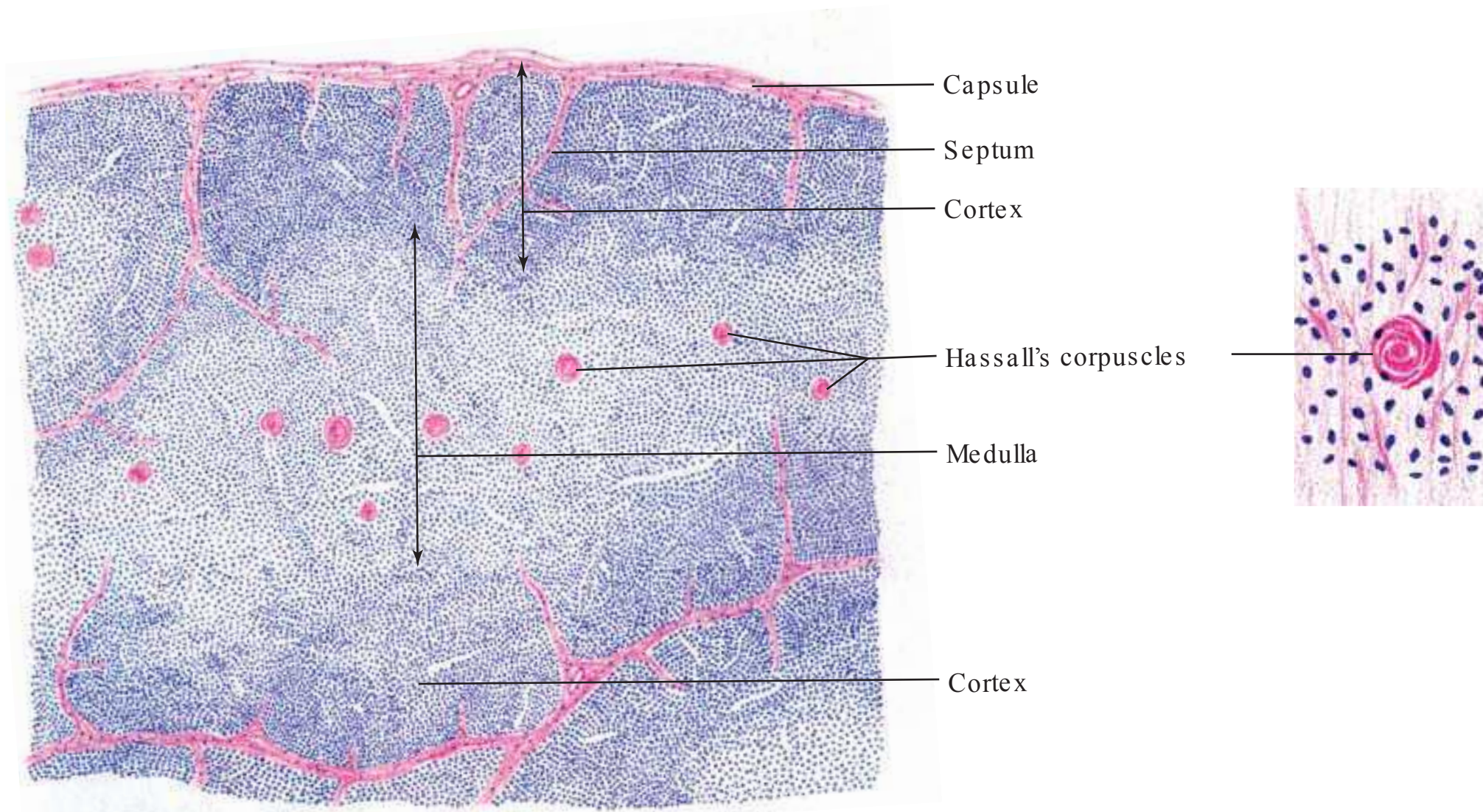
- Thymus has a capsule of connective tissue covering both the lobes.
- From the capsule, numerous septa containing blood vessels extend into the substance of the organ and divide the organ into incomplete lobules (Fig. 11.4; PMG 11.1).
- Each lobule consists of peripheral cortex and central medulla.
- Since the septa do not divide the organ completely, the central part (medulla) of each lobule is continuous with the medulla of the neighbouring lobules.

## Cortex

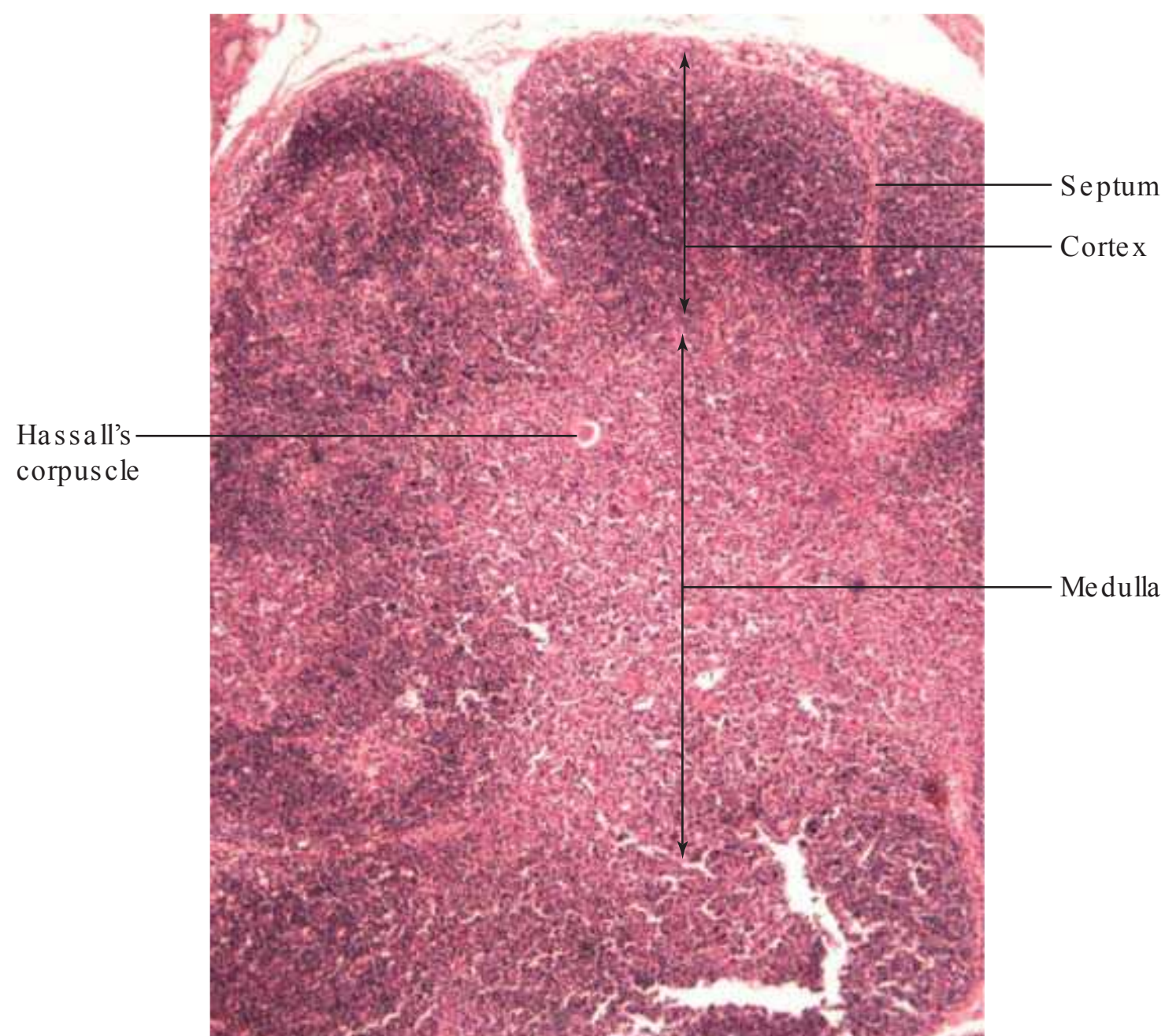
- Cortex is the peripheral dark zone of each lobule (Fig. 11.4; PMG 11.1).
- It is mainly composed of densely packed T lymphocytes. Apart from lymphocytes, cortex also contains epithelial reticular cells and macrophages.
- Most of the lymphocytes in cortex are small in size and immature; (they are known as thymocytes). Some large and medium-sized lymphocytes are also present. Macrophages phagocytose the degenerating lymphocytes. Epithelial reticular cells, also known as epitheliocytes, are derived from endoderm



(of the third pharyngeal pouch). These cells have large ovoid nuclei and long cytoplasmic processes. The cytoplasmic processes of adjacent cells are connected and form a meshwork. This meshwork provides support to the other cells of thymus.



**Figure 11.4** Section of thymus. Inset shows further enlarged view of Hassall's corpuscle. (H&E pencil drawing)

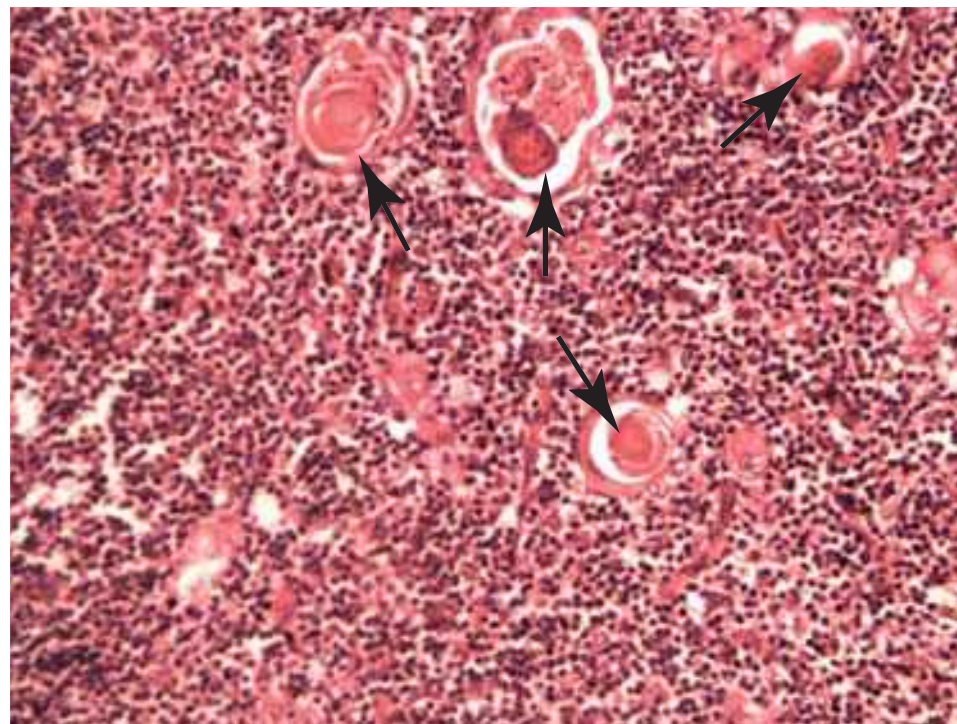


**PMG 11.1** Thymus (H&E stain, X10).



## Medulla

- Medulla is the central lighter zone of each lobule (Fig. 11.4; PMG 11.1); it contains less number of lymphocytes than cortex and hence appears lighter.
- Medulla of a lobule is continuous with the medulla of neighbouring lobules.
- Lymphocytes in medulla are fewer while epithelial reticular cells are more in number than those in the cortex. Lymphocytes are of mature variety.
- Prominent feature in medulla is Hassall's corpuscles, also known as thymic corpuscles (Fig. 11.4; PMG 11.1). They consist of concentrically arranged epitheliocytes (Fig. 11.4, inset; PMG 11.2).
- Lymphocytes proliferate in cortex and migrate into medulla, and from here they enter the systemic circulation and reach the various lymphoid organs.
- Epitheliocytes in medulla secrete the thymic hormones thymosin and thymopoietin. The cytoplasm of these epitheliocytes has secretory granules which contain these thymic hormones. These hormones promote T cell proliferation and maturation.



**PMG 11.2** Thymus—arrows indicate Hassall's corpuscles (H&E stain, X20).

## BLOOD–THYMUS BARRIER

- The antigen circulating in the blood does not come in contact with thymic lymphocytes due to the presence of blood–thymus barrier.
- This barrier consists of an endothelium of capillaries, a thick basement membrane and a layer of reticular epithelial cells.

## LYMPH NODE

- Lymph nodes are bean-shaped structures present in the course of the lymphatic vessels.
- Lymph passes through the lymph nodes before returning back into the systemic circulation.
- The concave surface of the lymph node has a depression called hilum. Lymphatic vessels and veins leave the lymph node while the artery enters it through the hilum.
- Functions
  - (a) Filtration of lymph
  - (b) Presentation of antigens to T cells to initiate immune response
  - (c) Lymphopoiesis (production and differentiation of lymphocytes)

## MICROSCOPIC FEATURES

- Lymph nodes have a capsule, cortex, medulla and various sinuses.



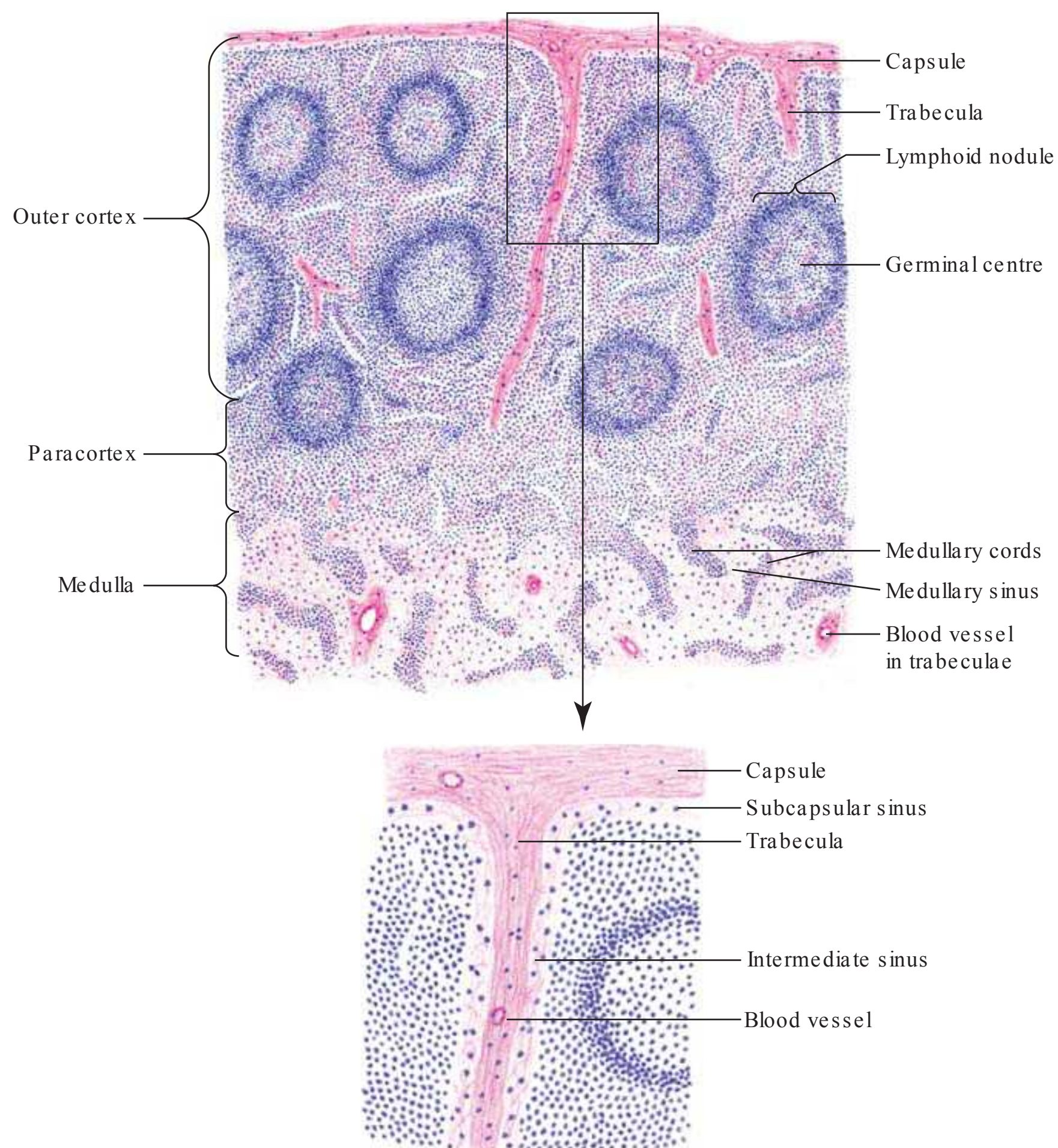
- Underneath the capsule, in the entire organ, reticular fibres which are produced by reticular cells form a three-dimensional network. This network of reticular fibres provides structural support to the cells of lymphoid tissue.

### Capsule (Fig. 11.5; PMG 11.3)

- The capsule is made up of connective tissue.
- It is pierced by afferent lymphatic vessels on the convex surface of the lymph node.
- Numerous trabeculae arise from the capsule and enter the substance of the node.

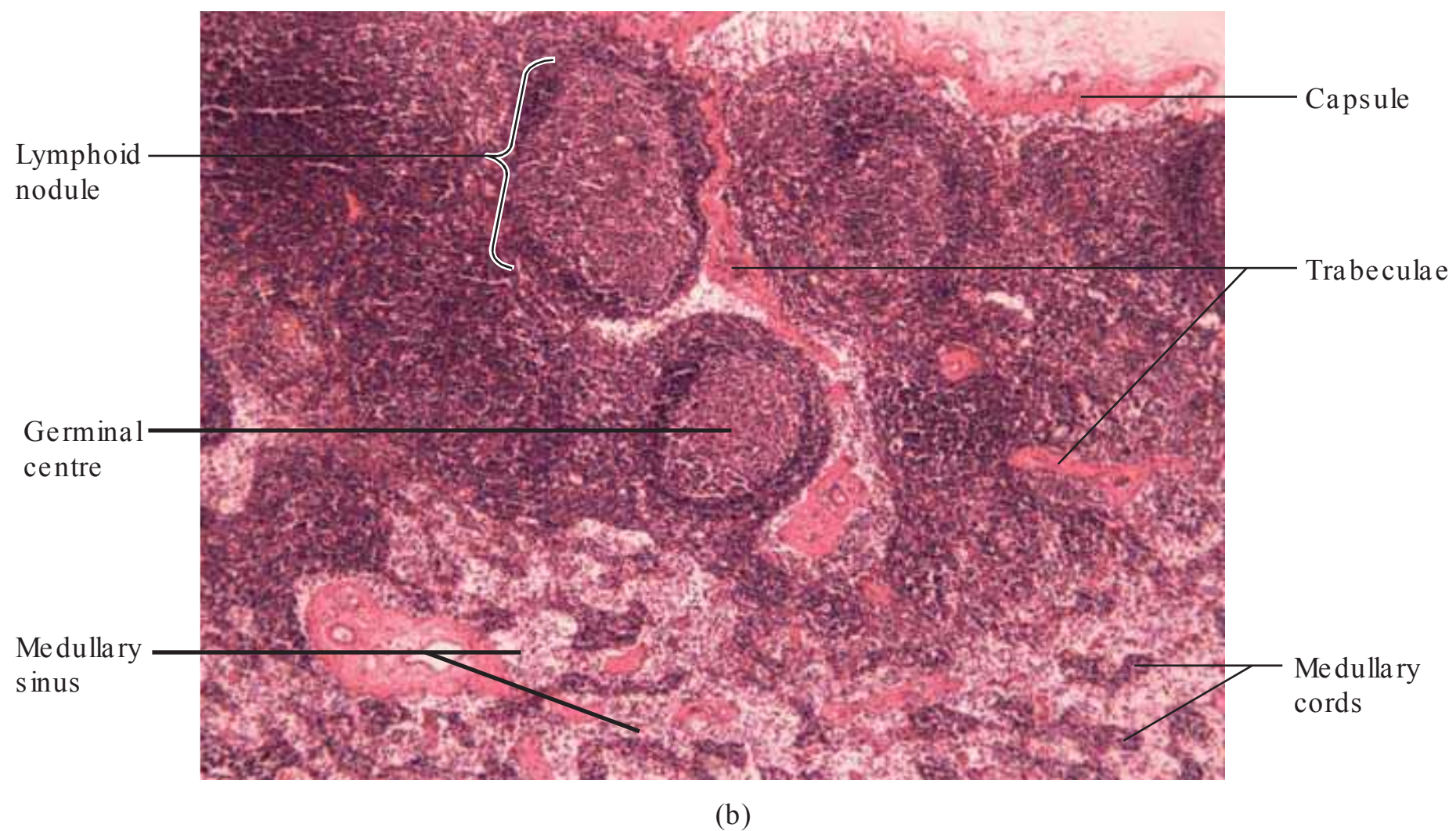
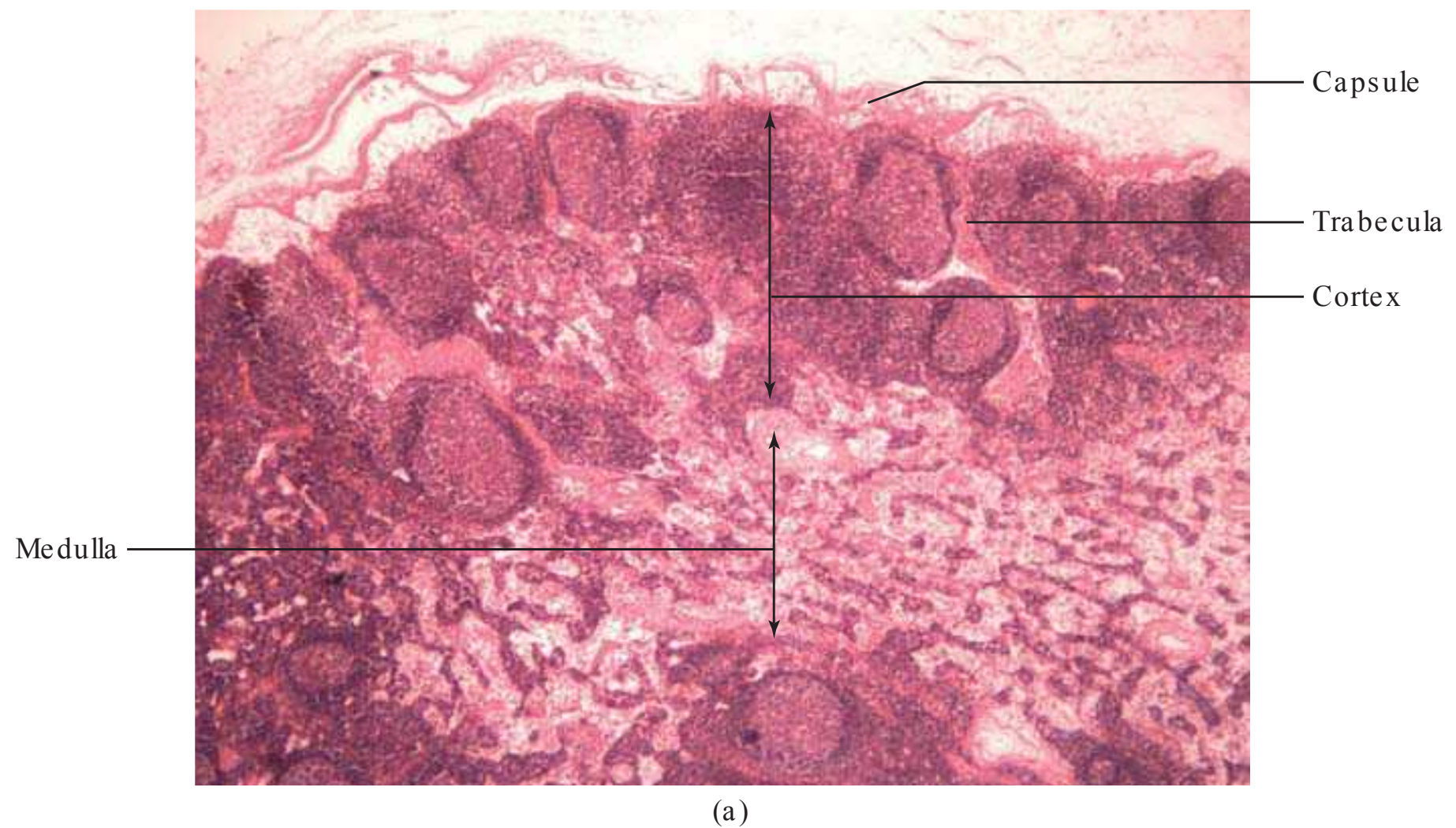
### Cortex (Fig. 11.5; PMG 11.3)

- Cortex is the darkly stained peripheral part of the lymph node, lying underneath the capsule. It is packed with lymphocytes. Plasma cells and macrophages are also present.
- It is divided into the outer cortex, which lies underneath the capsule, and the inner cortex, which lies underneath the outer cortex and surrounds the medulla.



**Figure 11.5** Section of lymph node in low magnification. Inset shows a further enlarged view of cortex; subcapsular and intermediate sinuses can be seen. (H&E pencil drawing)





**PMG 11.3** Lymph node: (a) X5 and (b) X10 (H&Estain).

### *Outer Cortex*

- The outer cortex contains mainly B lymphocytes which are arranged as spherical lymphoid nodules (Fig. 11.5). Some of these nodules show a light-stained zone in the centre called germinal centre, which is the site of B lymphocyte proliferation.
- The outer cortex also has antigen-presenting cells, the follicular dendritic cells.

### *Inner Cortex*

- The inner cortex is the inner zone of cortex; it is also known as paracortex.
- It has mainly T lymphocytes; hence, the inner cortex is also known as thymus-dependent cortex. No lymphoid nodule is seen in paracortex.
- It should be noted that the cells mentioned in the inner and outer cortices are the predominant cells in that particular region; apart from these cells, other cells of the lymphoid tissues are also present.



**Medulla** (Fig. 11.5; PMG 11.3)

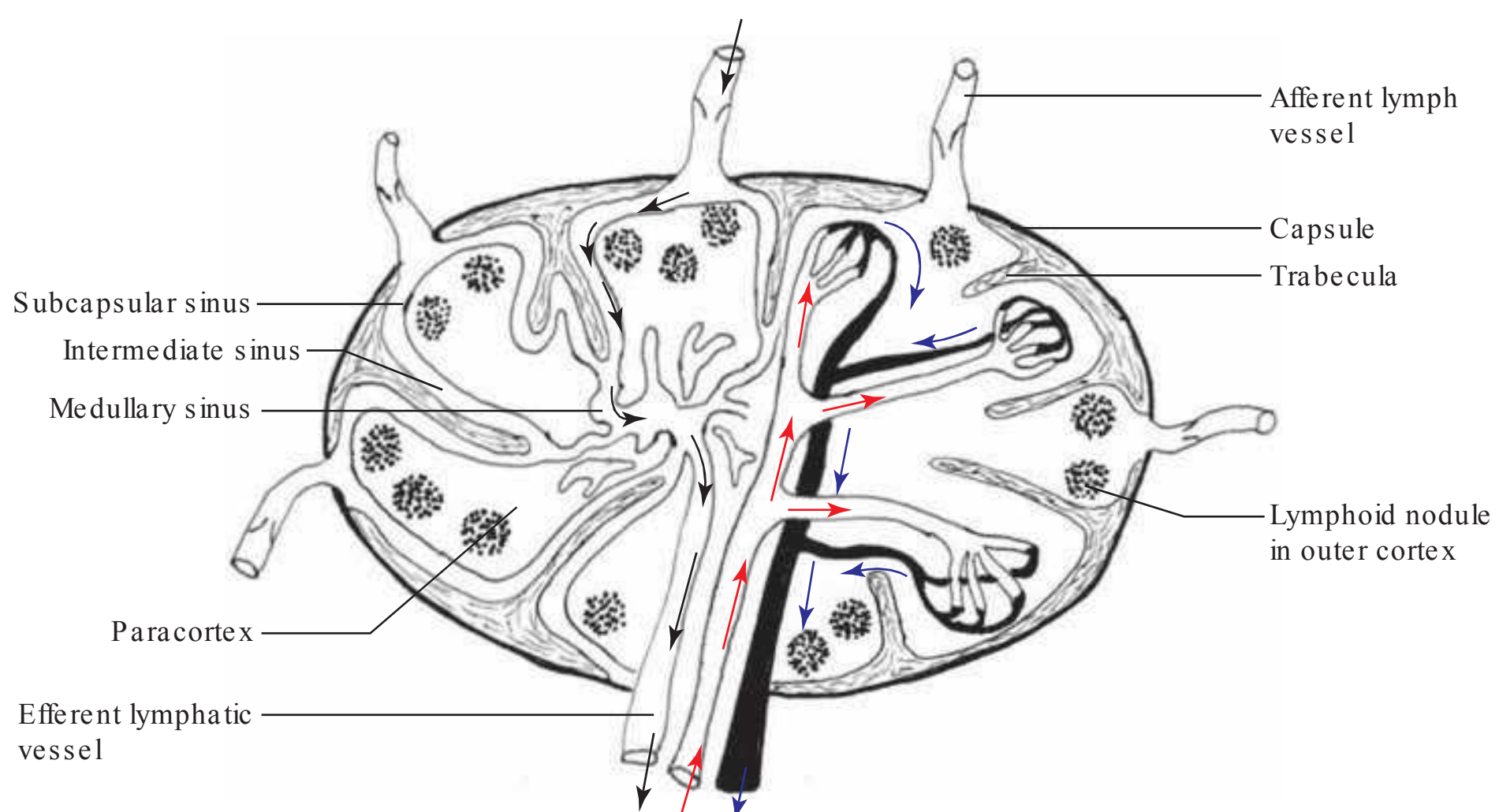
- Medulla is the light-stained central part of the lymph node.
- It consists of medullary cords and sinuses.
- Medullary cords are extensions of the inner cortex separated by medullary sinuses.
- Medullary cords have mainly B lymphocytes. Plasma cells and macrophages are also present.

**Sinuses** (Figs 11.5 and 11.6)

- Lymph passes through various sinuses of lymph nodes and gets filtered in them.
  - (a) Subcapsular sinus: It is present between the capsule and the outer cortex; it receives lymph from afferent lymphatic vessels.
  - (b) Intermediate sinus: It is present on both sides of the trabeculae and connects subcapsular sinus to medullary sinuses. It is also known as trabecular or peritrabecular sinus.
  - (c) Medullary sinuses: These are anastomosing sinuses present in between the medullary cords in the medulla.
- Inside the sinuses, reticular cells and fibres criss-cross the lumen and form a network through which the lymph percolates. Numerous macrophages are present in the reticular network. Processes of macrophages present outside the sinuses enter into the sinus through the wall of the sinus. The reticular network acts as a filter; the cellular debris carried by lymph gets trapped in the network and it is engulfed by the macrophages.
- Antigens are also trapped in the reticular network of sinuses. They are taken up by follicular dendritic cells (antigen-presenting cells) and presented to T cells to initiate immune response.

**LYMPH AND BLOOD CIRCULATION IN LYMPH NODE** (Fig. 11.6)

- Afferent lymphatic vessels pierce the capsule and drain into the subcapsular sinus, and from the subcapsular sinus lymph drains into the medullary sinus through the intermediate sinus. From medullary sinus, it drains into the efferent lymphatic vessel which leaves the lymph node through hilum.
- Arteries enter and veins leave the lymph node through hilum. Arteries branch and form a capillary network in cortex and medullary cords.

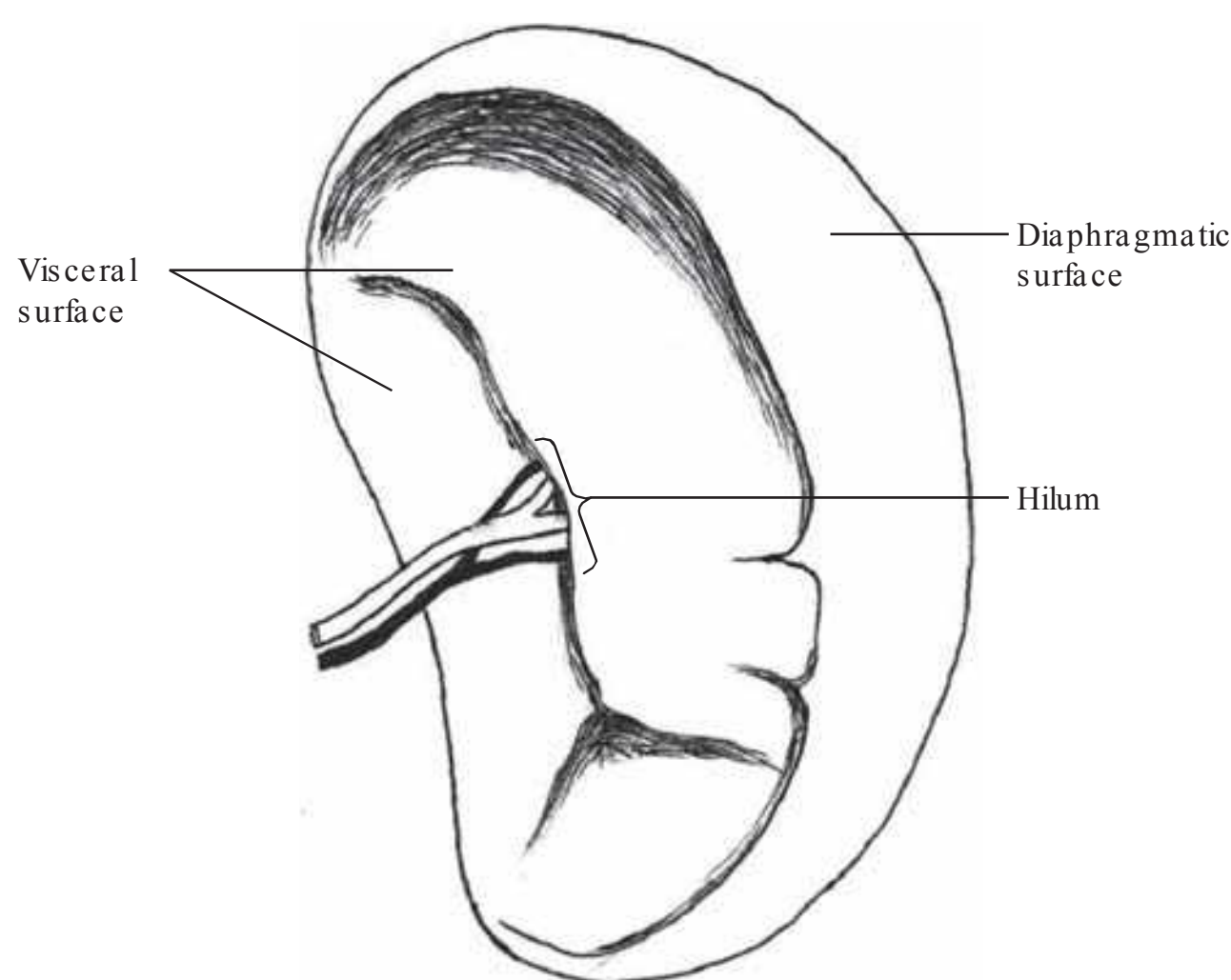


**Figure 11.6** Schematic diagram of a lymph node. The left half shows lymphatic circulation (black arrows) and the right half shows arterial (red arrows) and venous (blue arrows) circulation.



## SPLEEN

- Spleen is the largest lymphoid organ.
- It is located in the upper left part of the abdomen (Fig. 11.2).
- It has two surfaces—the diaphragmatic surface facing the diaphragm and the visceral surface facing the visceral organs (Fig. 11.7). The visceral surface has the hilum through which splenic vessels pass.
- Functions
  - (a) Spleen is responsible for removal of aged and defective erythrocytes and foreign particles.
  - (b) It is the site of immune reactions to blood-borne antigens.
  - (c) It is involved in lymphopoiesis.
  - (d) In embryonic life, it is one of the sites for haemopoiesis.



**Figure 11.7** Spleen.

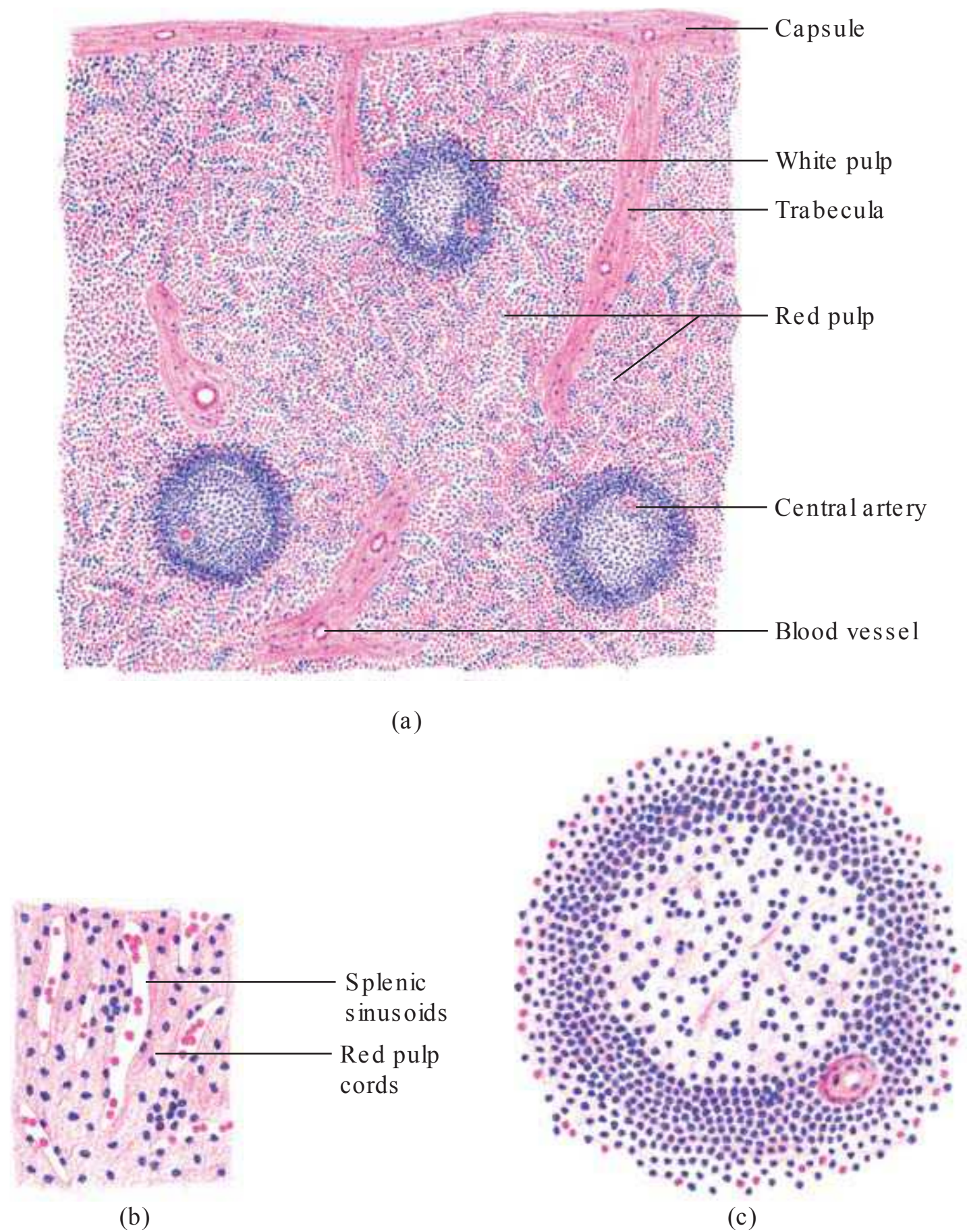
## MICROSCOPIC FEATURES

- Spleen is covered by a capsule. The parenchyma of the spleen consists of white pulp, red pulp and a marginal zone. The terms red pulp and white pulp are based on the appearance of the unstained sections of fresh specimen. In the unstained section of fresh specimen, there are grey-coloured circular regions (white pulp) surrounded by dark red tissue (red pulp).
- Unlike lymph nodes, spleen does not have afferent lymphatics. Also, the lymphatic tissue is not present as cortex and medulla; instead, it has white pulp and red pulp (Fig. 11.8; PMG 11.4).
- Like other lymphoid organs, spleen also has a network of reticular fibres providing structural support to the cells of lymphoid tissue.

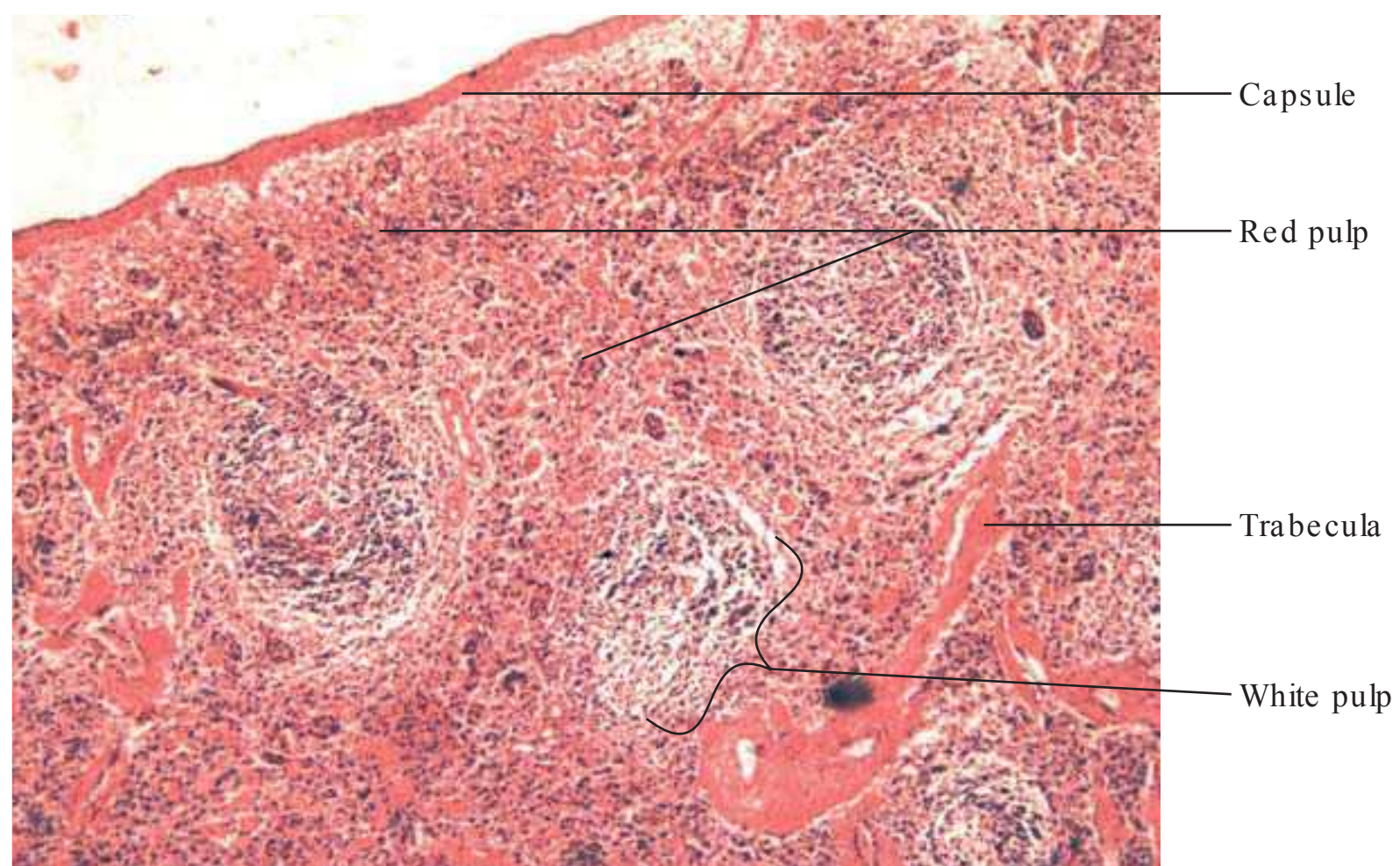
### Capsule

Spleen has a capsule of dense connective tissue from which trabeculae arise and enter the substance of the organ. Blood vessels present in trabeculae also enter the organ along with it (Fig. 11.8; PMG 11.4).





**Figure 11.8** Section of spleen in (a) low magnification, (b) high magnification—red pulp and (c) high magnification—white pulp (H&E pencil drawing).

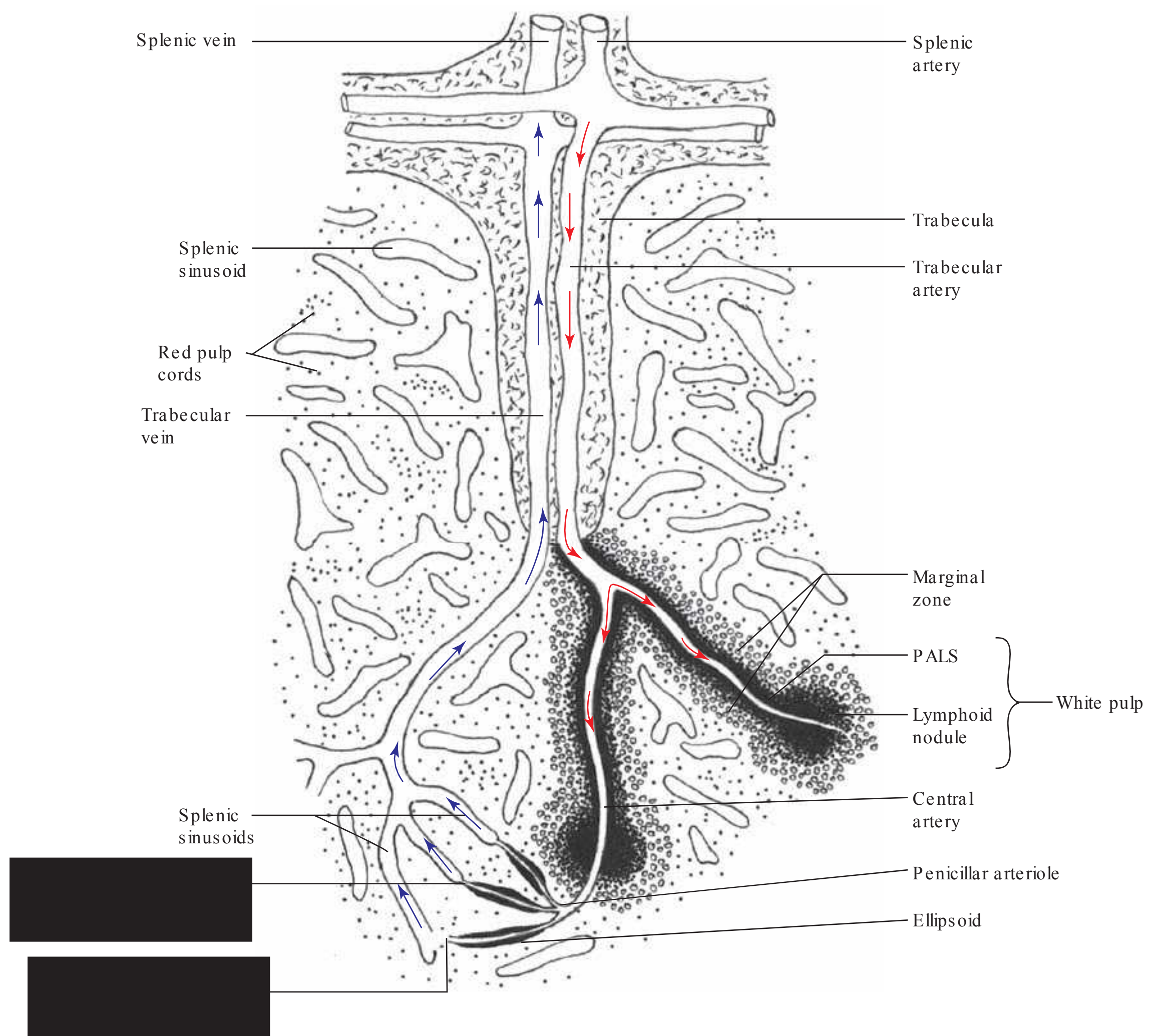


**PMG 11.4** Spleen (H&E stain, X10).



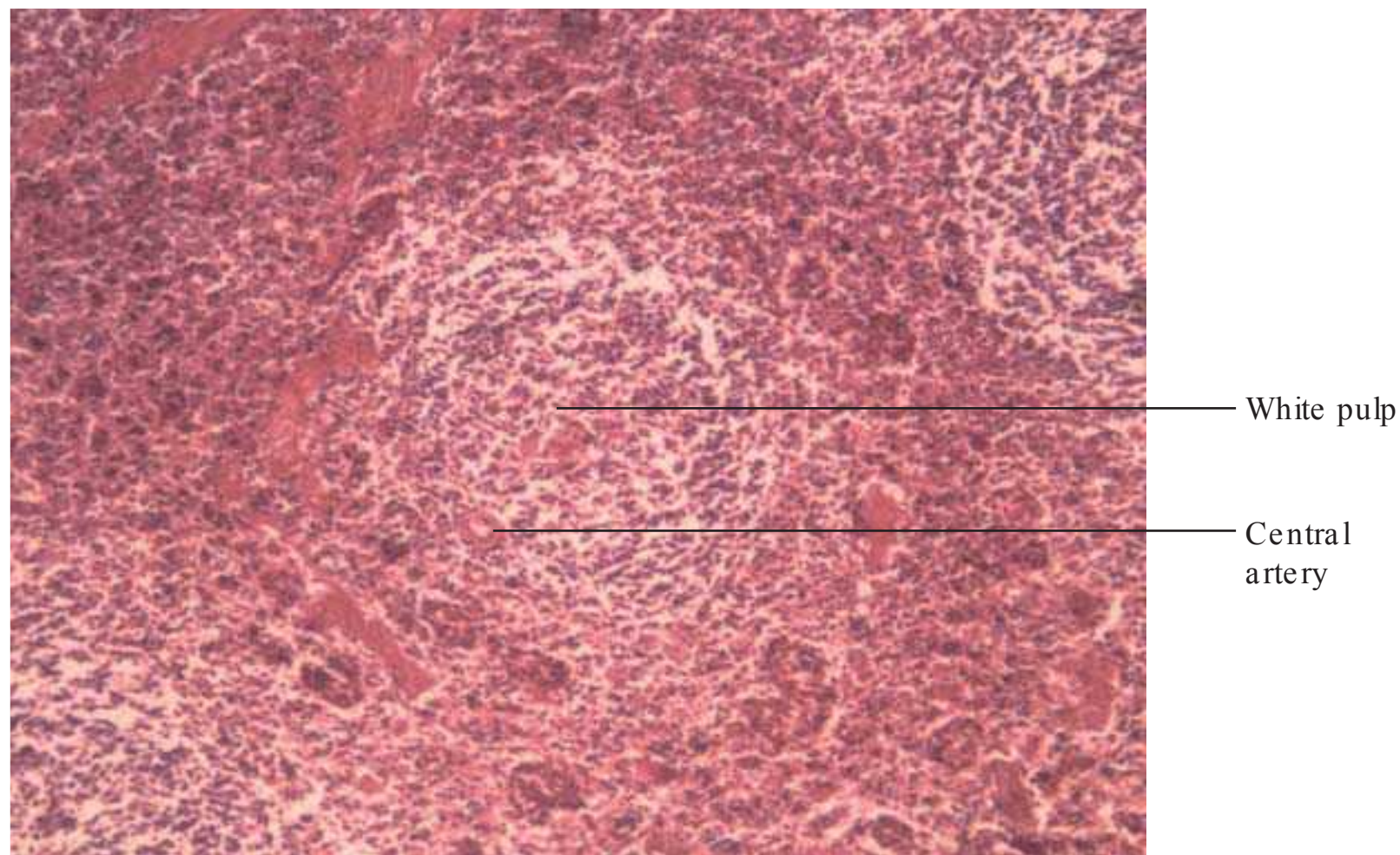
**White Pulp** (Figs 11.8 and 11.9; PMG 11.4 and 11.5)

- Arteries in trabeculae give rise to arterioles. These arterioles, known as central arteries, leave trabeculae and enter the parenchyma of spleen.
- In the parenchyma, a sheath of lymphoid tissue surrounds the central arteries. These sheaths of lymphoid tissues are called periarterial lymphatic sheaths (PALS) (Fig. 11.9).
- It contains mainly T cells; thus, PALS is the thymus-dependent zone of spleen.
- Along the course of PALS, at some places PALS expands to form lymphoid nodules (known as splenic nodules or Malpighian corpuscles) (Fig. 11.8). They mainly contain B cells and some of these follicles show germinal centre.
- PALS and the Malpighian corpuscle together form the white pulp.
- In PALS, the central artery is in the centre, whereas in splenic nodules it is eccentric in position.



**Figure 11.9** Schematic diagram of splenic circulation. Arterial circulation is shown by red arrows and venous drainage by blue arrows. PALS, periarterial lymphatic sheath.





**PMG 11.5** White pulp of spleen (H&E stain, X20).

### **Red Pulp** (Figs 11.8 and 11.9; PMG 11.4)

- Most of the spleen consists of red pulp.
- It has two components—red pulp cords and sinusoids (Fig. 11.8b).
- Red pulp cords are also called cords of Billroth. They are irregular anastomosing cords surrounding the sinusoids. They consist of mainly reticular cells and erythrocytes. Macrophages, plasma cells and lymphocytes are also present.
- Splenic sinusoids have wide lumen; the endothelial cells of sinusoids are elongated and lie parallel to the longitudinal axis of the sinusoids. Neighbouring endothelial cells have gaps through which blood cells can pass. Processes of macrophages (present in red pulp cords) also enter the lumina of the sinusoids through these gaps. The basal lamina of the sinusoid is discontinuous.

### **Marginal Zone**

- Marginal zone is located at the periphery of PALS, that is between the red and white pulps.
- It consists of a reticular network of blood sinusoids, lymphocytes and antigen-presenting follicular dendritic cells.
- The role of marginal zone is to trap the blood-borne antigen from the circulation and present it to the lymphocytes of the spleen.

### **SPLENIC CIRCULATION** (Fig. 11.9)

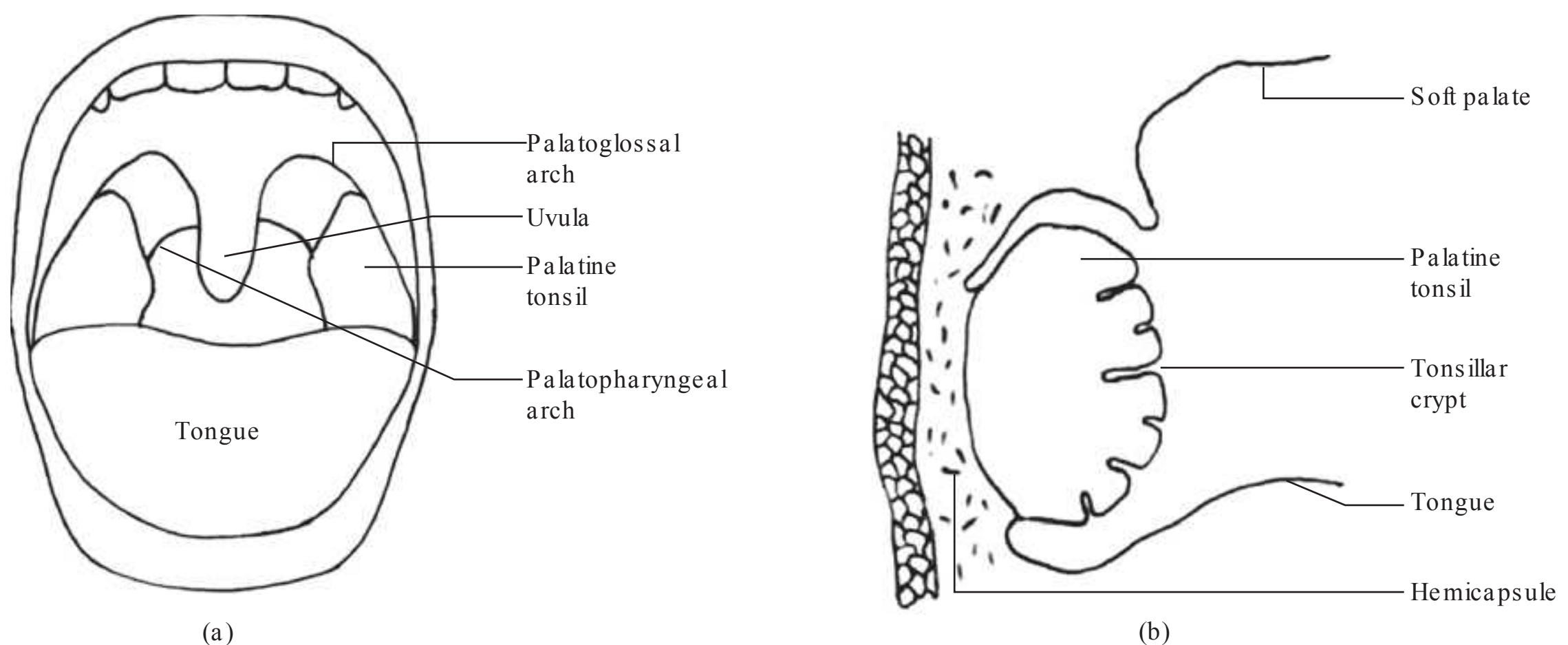
- The splenic artery enters the organ through the hilum and divides into numerous trabecular arteries which enter the trabeculae.
- The trabecular arteries give off many arterioles which leave the trabeculae and enter the parenchyma of the organ.
- In the parenchyma, these arterioles pass through the white pulp. As mentioned earlier, in PALS the central artery occupies central position and in splenic nodules it is eccentric in position.
- The central artery leaves the white pulp and enters the red pulp where it divides into numerous branches. Since these branches are straight, they are called penicillar arterioles.
- Penicillar arterioles give numerous branches which pass through a sheath of macrophages called ellipsoid.



- The penicillar arteriole becomes a capillary after passing through ellipsoid. These capillaries carry the blood to the sinusoids present in between the red pulp cords. There are two theories which explain how the blood from the capillaries reaches the sinusoids.
  - (a) Closed theory: According to this theory, the capillaries open directly into the sinusoids and the blood remains inside the blood vessel.
  - (b) Open theory: According to this theory, the capillaries open into the red pulp cords, and the blood passes through the red pulp cords and then enters the sinusoids. This circulation is predominant in humans.
- Sinusoids drain into trabecular veins and trabecular veins drain into the splenic vein.

## PALATINE TONSIL

- The palatine tonsil is a pair of lymphoid tissue located in the lateral wall of oropharynx. It is located in the tonsillar sinus between palatoglossal and palatopharyngeal folds (Fig. 11.10a).
- The palatine tonsil has medial (or luminal) and lateral surfaces. The medial surface is covered with the mucosa of the oral cavity and the lateral surface has a hemicapsule (called so since it is present only on one surface of the organ). The mucosa covering its luminal surface invaginates into the substance of the organ and forms crypts; there are 15–20 crypts (Fig. 11.10b).

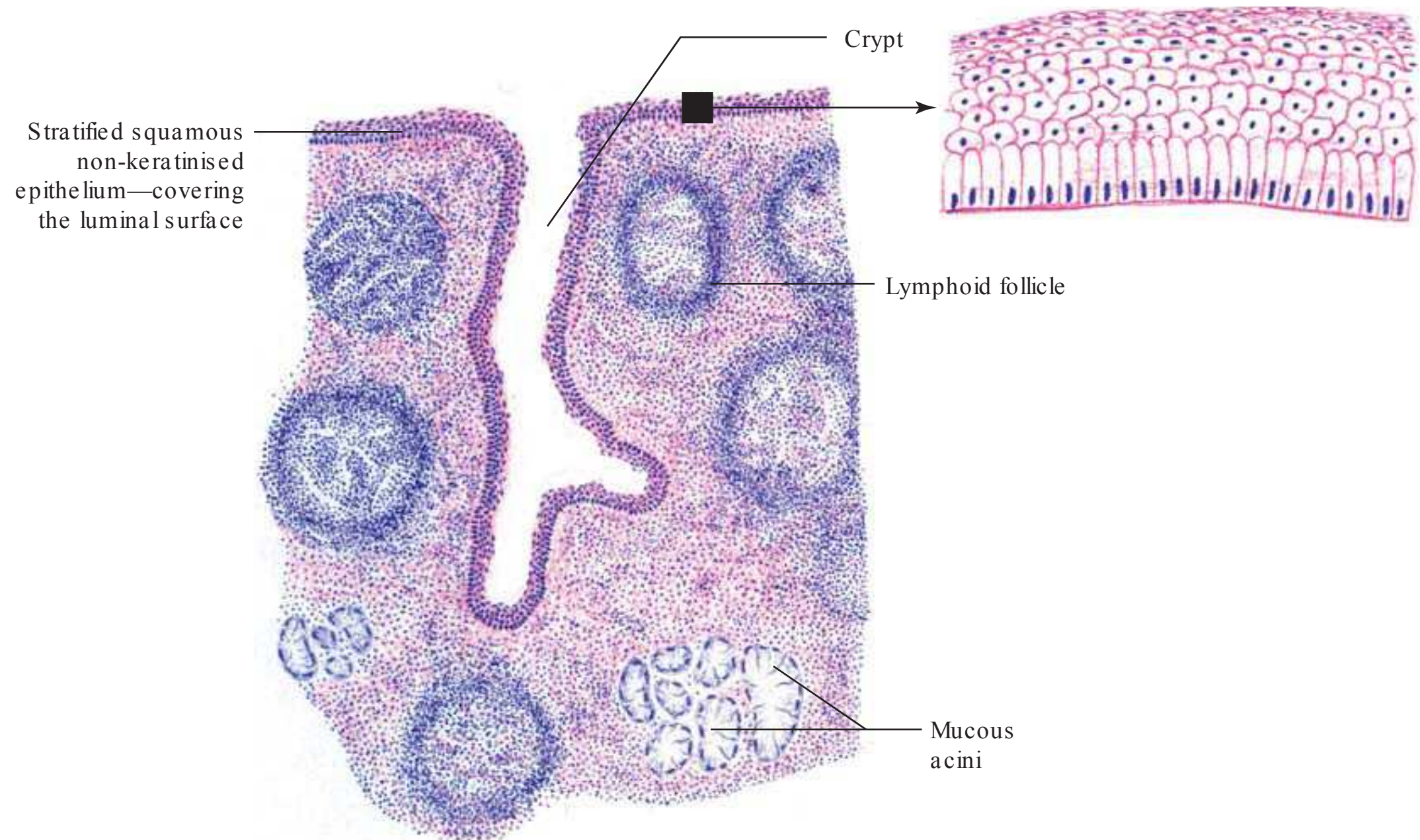


**Figure 11.10** Palatine tonsil: (a) location of palatine tonsil in oropharynx and (b) palatine tonsil in coronal section of oropharynx.

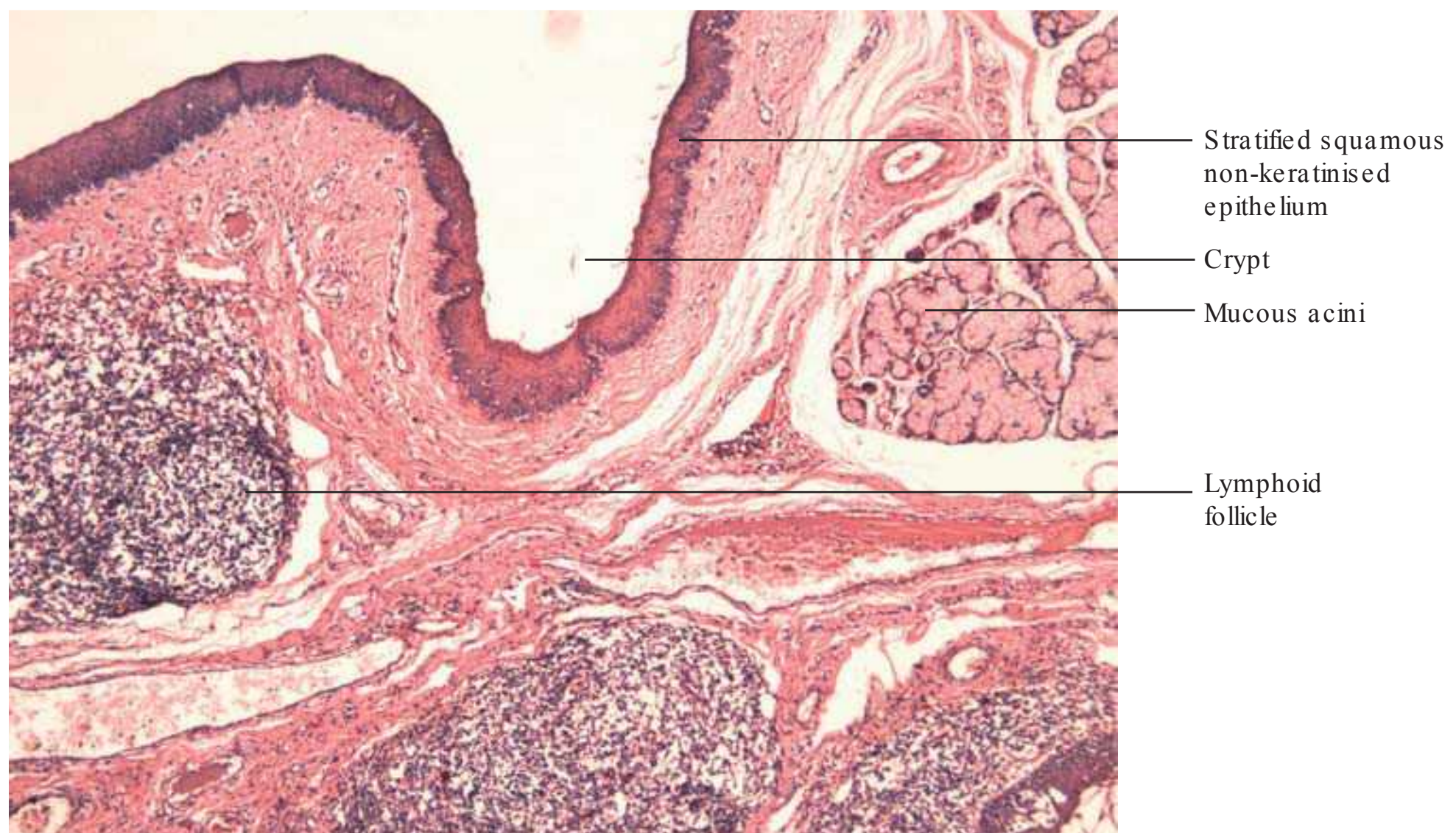
## MICROSCOPIC FEATURES

- The medial surface (facing the lumen of oropharynx) and crypts of the palatine tonsil are lined by stratified squamous non-keratinised epithelium (Fig. 11.11; PMG 11.6).
- Underneath the crypts, there are numerous lymphoid follicles.
- The lateral surface of the palatine tonsil is separated from the underlying tissues by a hemicapsule.





**Figure 11.11** Section of palatine tonsil in low magnification. Inset shows an enlarged view of stratified squamous non-keratinised epithelium. (H&E pencil drawing)



**PMG 11.6** Palatine tonsil (H&E stain, X10).



## CLINICAL CORRELATES

### DiGeorge Syndrome

- DiGeorge syndrome is a rare congenital disease. It occurs due to the absence of thymus and parathyroid gland. Due to the absence of thymus, T lymphocytes are reduced and there is abnormal cell-mediated immunity. Humoral immunity is however normal, as B lymphocyte levels are normal.

### Thymoma

- Thymoma is the tumour of thymus; it can be benign or malignant.

### Metastasis

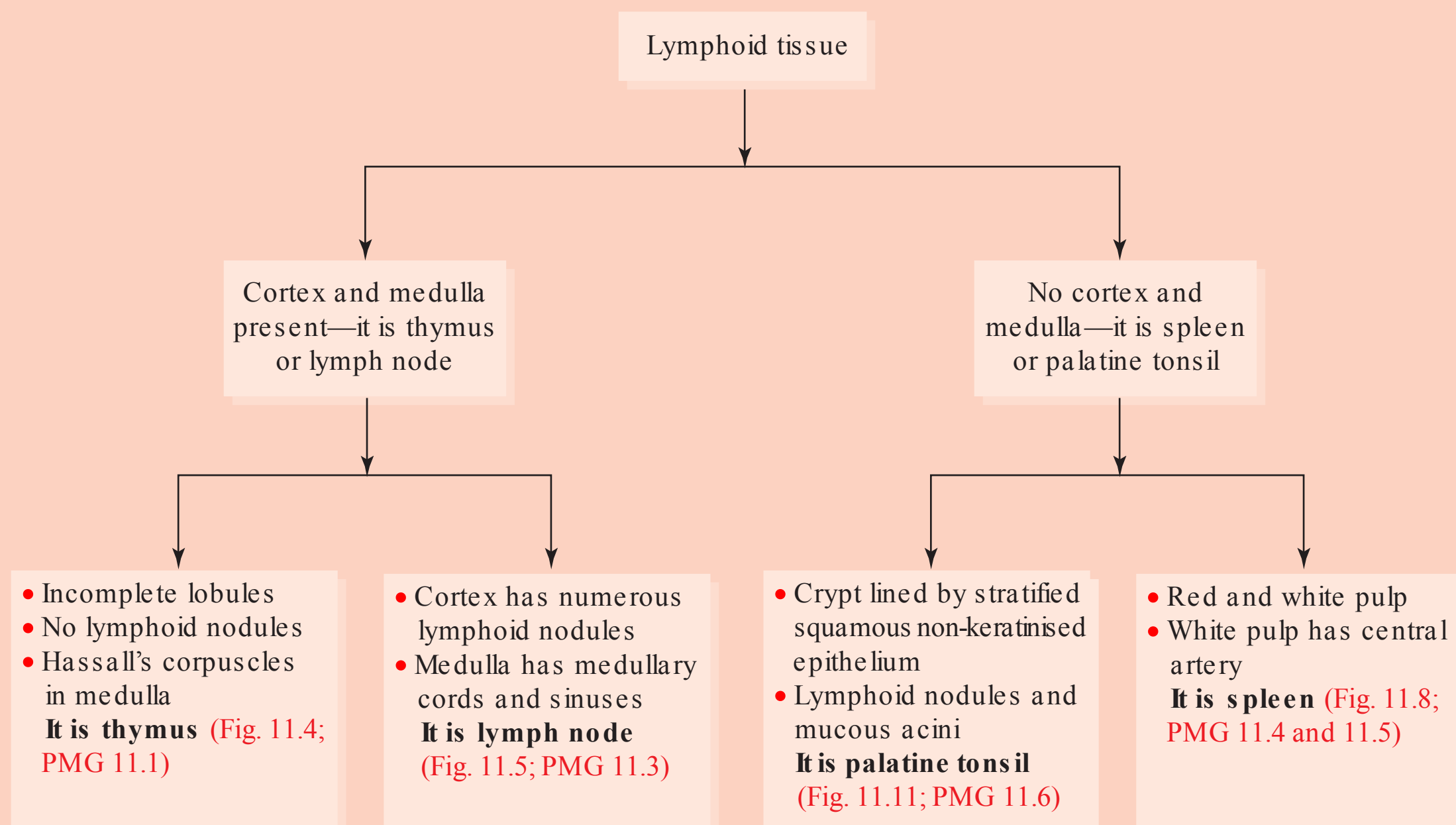
- Spread of cancer to other parts of the body is called metastasis. Most common route for this spread is via lymphatic vessels. Through the lymphatic vessels the cancer spreads to lymph nodes. Affected lymph nodes enlarge in size and become hard in consistency.

### Lymphadenitis

- Inflammation of the lymph node is called lymphadenitis. In acute cases, lymph nodes become enlarged and painful. Enlargement is due to leucocytic infiltration and oedema (accumulation of fluid). This causes stretching of the capsule, which is painful.

## KEYPOINTS

### Key Points for Histology Slide Identification



## Lymphoid Organs

Thymus and bone marrow are primary lymphoid organs, while other lymphoid organs are secondary lymphoid organs.

Features	Thymus	Lymph node
Capsule and trabeculae	Both are present; trabeculae divide it into incomplete lobules	<ul style="list-style-type: none"> <li>Both are present; underneath the capsule is subcapsular sinus and on the sides of trabeculae are intermediate sinuses</li> </ul>
Cortex	It has immature T lymphocytes	<ul style="list-style-type: none"> <li>The outer cortex has B lymphocytes</li> <li>The inner cortex has T lymphocytes</li> <li>The lymphoid nodule is only in the outer cortex</li> </ul>
Medulla	It has mature T lymphocytes and Hassall's corpuscles	<ul style="list-style-type: none"> <li>It has medullary cords separated by medullary sinuses</li> <li>Medullary cords have B lymphocytes</li> </ul>

## Spleen

Capsule and trabeculae	Both are present; blood vessels pass through them and supply the parenchyma
White pulp	It includes PALS and splenic nodules
Red pulp	It includes red pulp cords and sinusoids

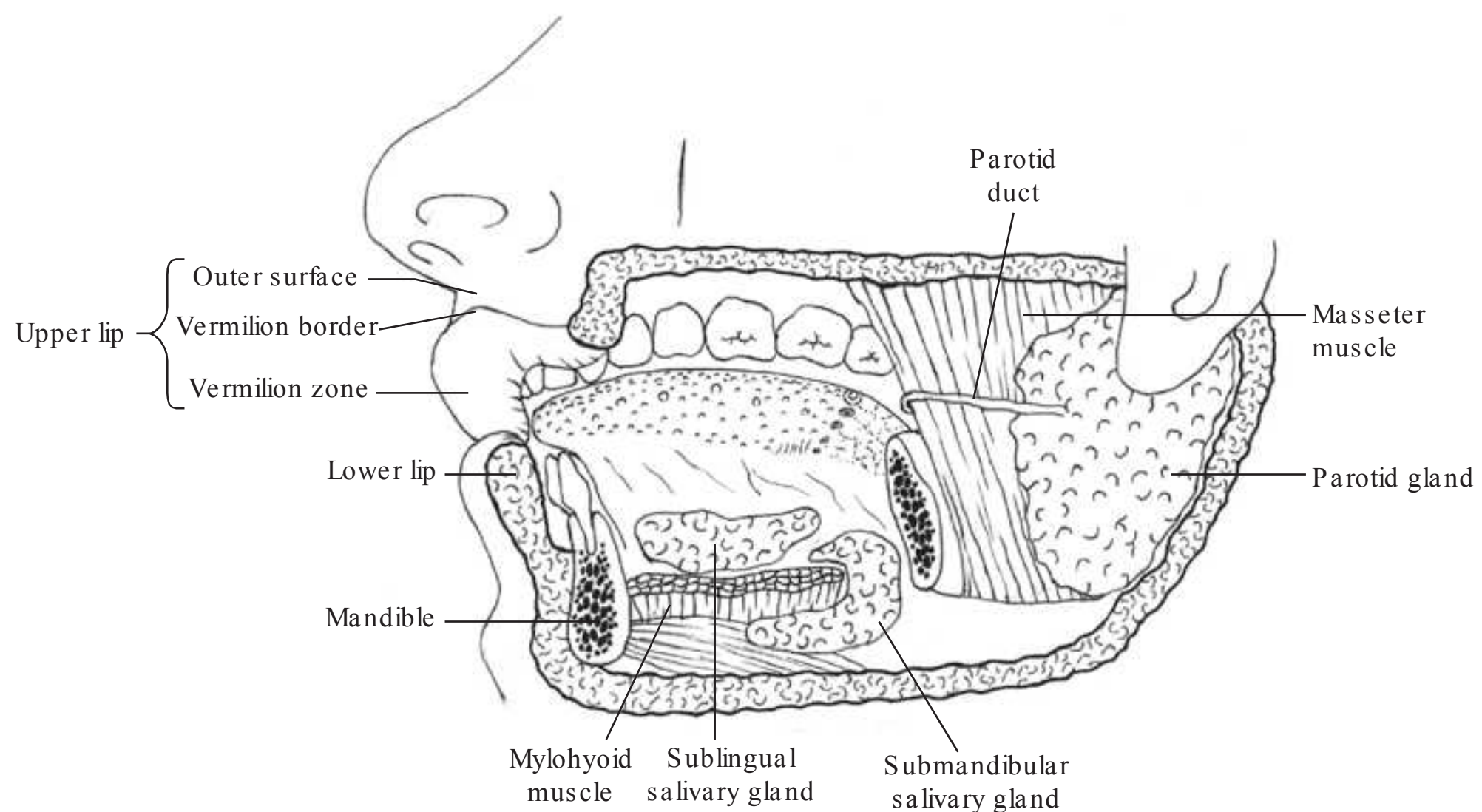
## SELF-ASSESSMENT

1. How are lymphoid organs classified?
2. What are Hassall's corpuscles?
3. Name the lymphoid organs that have cortex and medulla?
4. What are the types of lymphocytes in the outer and inner cortices of lymph nodes?
5. What are the components of the medulla of a lymph node?
6. What are the types of sinuses present in the lymph node?
7. Describe the splenic circulation. What are the components of red and white pulps?
8. What are the thymus-dependent zones of lymph node and spleen?
9. Tonsillar crypt is lined by which type of epithelium?



# Oral Cavity

- The gastrointestinal tract is a hollow tract which begins from the oral cavity and ends at the anus.
- The oral cavity consists of lips, teeth, gums, cheeks, tongue, palate, salivary glands (Fig. 12.1) and tonsils.
- The ducts of all salivary glands open in the oral cavity. The microscopic structure of the salivary gland is described in Chapter 14.



**Figure 12.1** Oral cavity and its contents.

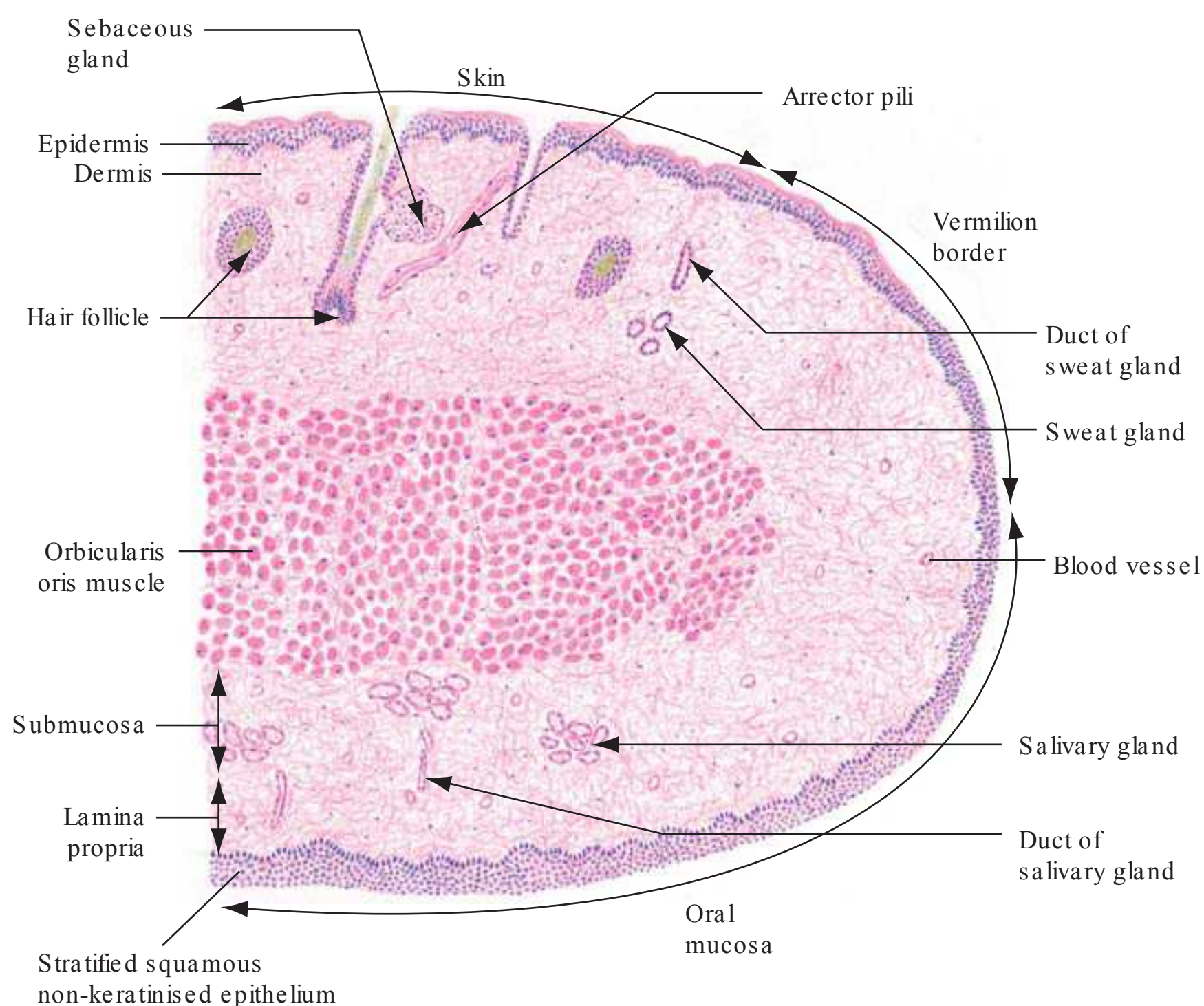
- Functions: Functions of the oral cavity are as follows:
  - (a) **T**eeth help in breaking the large food particles into smaller ones by chewing and thereby make it suitable for swallowing.
  - (b) Salivary glands secrete saliva which helps in lubrication. Digestive enzymes present in saliva begin the digestive process.
  - (c) The tongue helps in taste perception, swallowing, chewing and in speech.
  - (d) **T**onsils provide immunological protection against invasion by pathogens.
  - (e) Apart from the above-mentioned functions, the oral cavity is also responsible for speech.

## ORAL MUCOSA

- The entire oral cavity is lined by oral mucosa, which consists of the lining epithelium and underlying lamina propria. The mucosa gets modified according to the functional needs of the different parts of the oral cavity.
- The oral cavity is lined by stratified squamous epithelium which is mostly non-keratinised. The epithelium becomes keratinised on the hard palate, gums and filiform papillae of the tongue as these areas of the oral cavity are subjected to mechanical stress while chewing.
- The epithelium rests on lamina propria which consists of connective tissue.
- Underneath the mucosa is a layer of loose connective tissue, the submucosa, which provides mobility to oral mucosa. In particular areas of the oral cavity which are subjected to mechanical stress while chewing (the hard palate, gums and the tongue), the oral mucosa is not mobile. This is because these areas lack submucosa, and the mucosa is directly anchored to the underlying bone or muscle. In the regions where the mucosa is directly attached to the periosteum of the bone, both layers are collectively called mucoperiosteum.

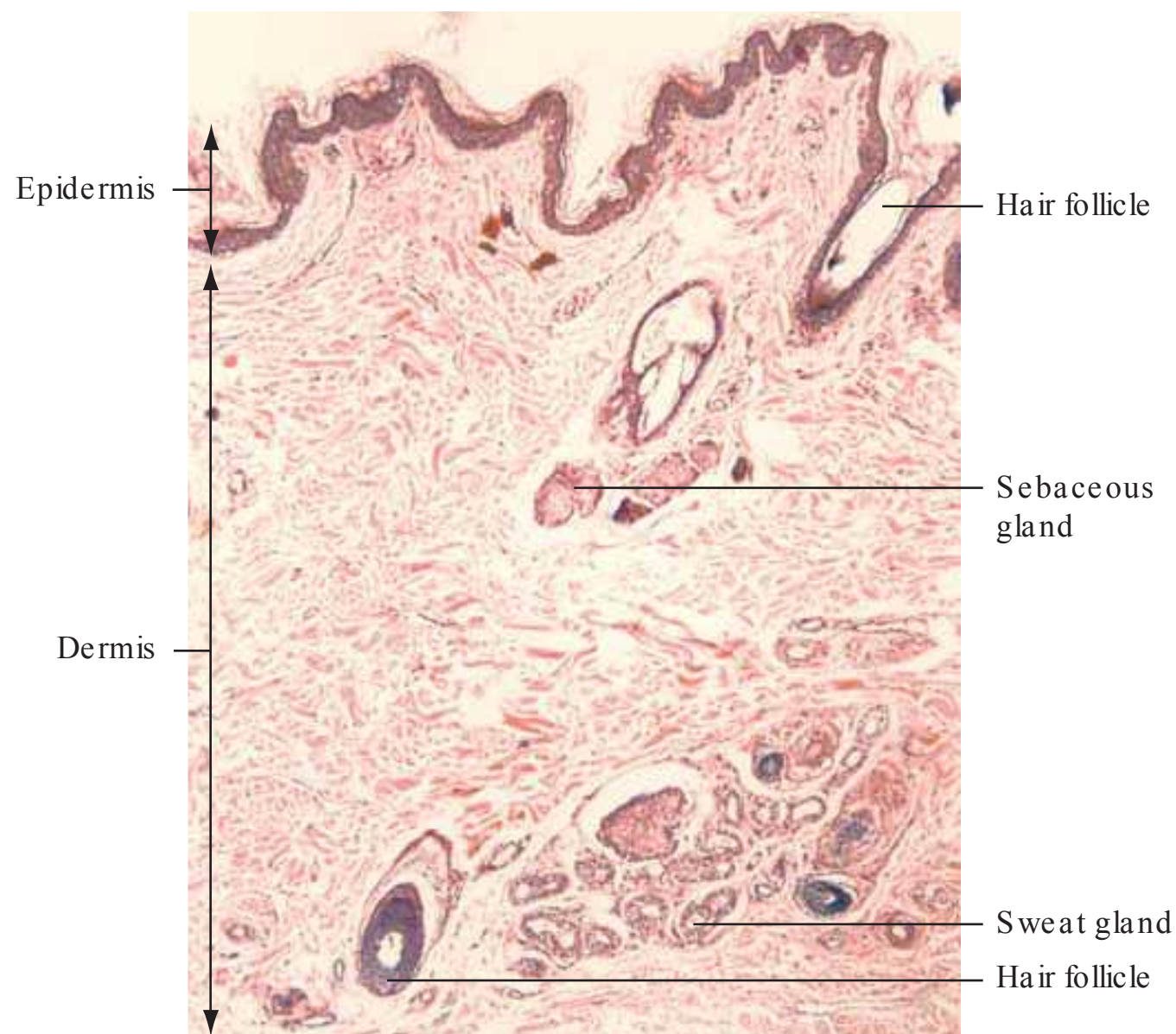
## LIPS

- Lips are folds of soft tissue that surround the opening of the oral cavity.
- Lips have three surfaces, namely outer, inner and vermilion zone (Figs 12.1 and 12.2). The outer surface is covered by skin. The inner surface of the lip is not visible when the mouth is closed and can only be seen in an open mouth. In between the outer and inner surfaces, there is a zone of transition called



**Figure 12.2** Section of lip in low magnification (H&E pencil drawing).

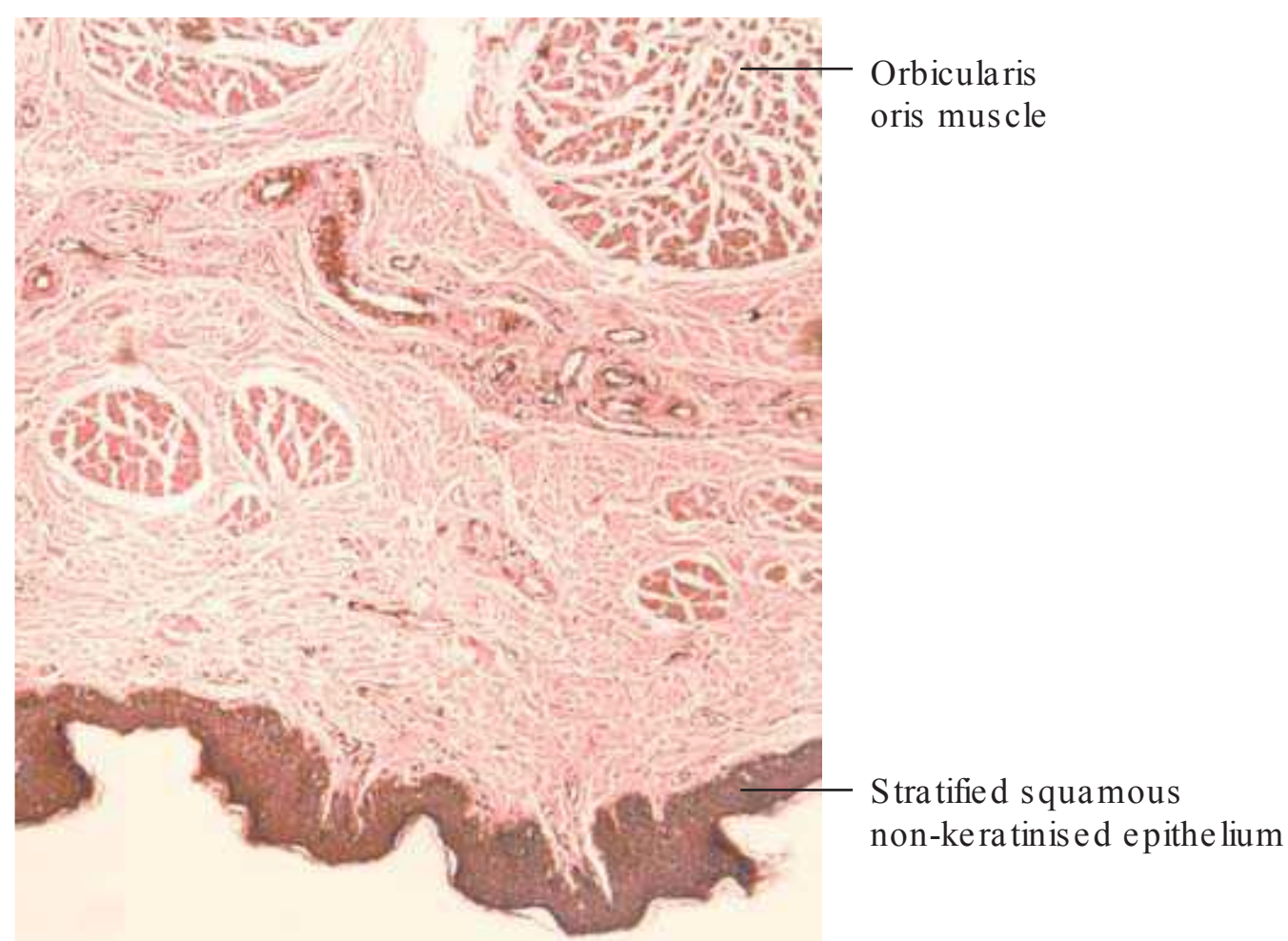




**PMG 12.1** Lip—outer surface (H&E stain, X10).

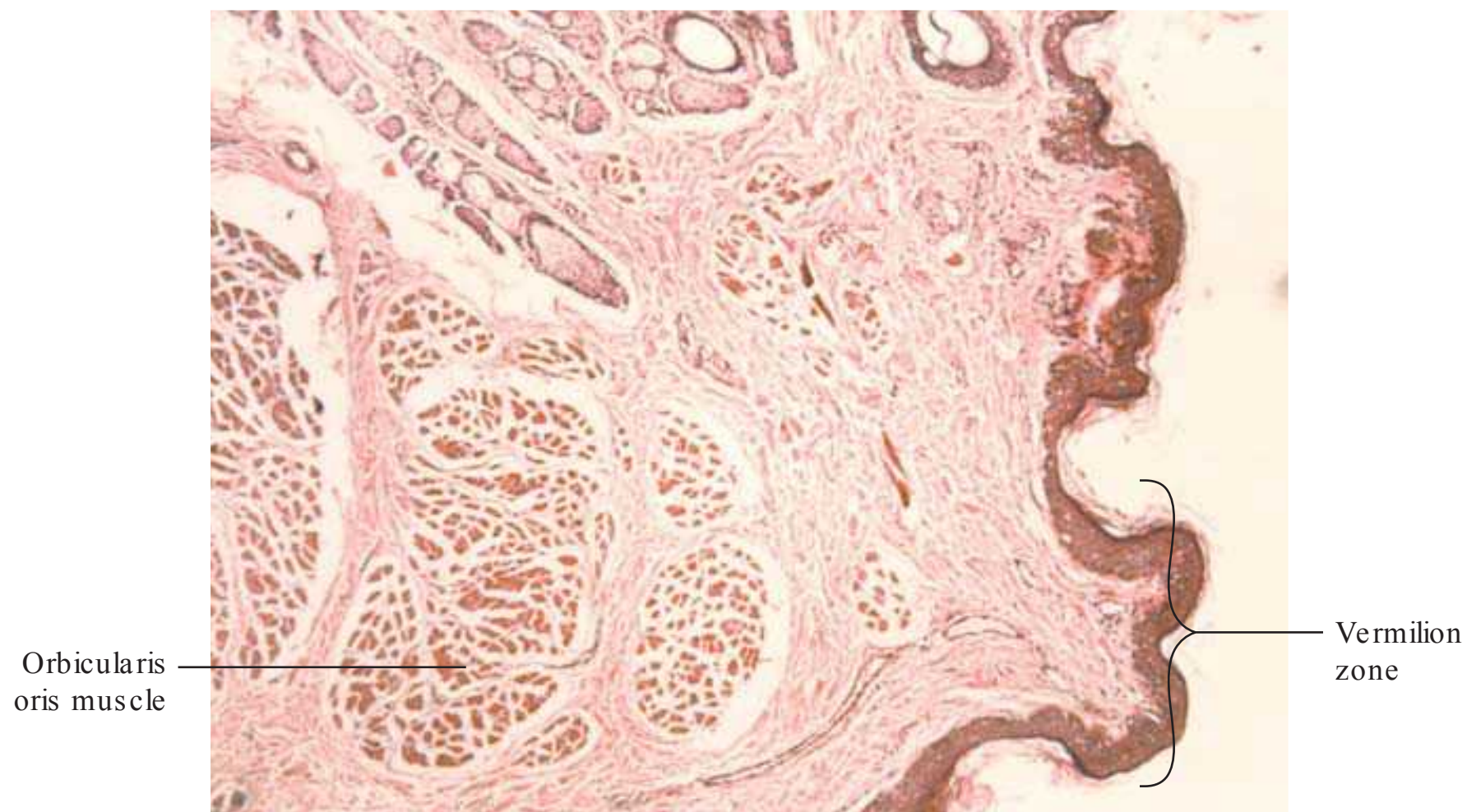
vermilion zone. It is this surface which a layman considers as lip. The junction of the outer surface (which is lined by skin) and the vermilion zone is vermilion border (Fig. 12.1).

- The outer surface is covered by skin which is hairy, having sebaceous and sweat glands (Fig. 12.2; PMG 12.1). The inner surface is covered by oral mucosa (Fig. 12.2; PMG 12.2). The vermilion zone is lined by modified skin which does not have glands and hairs (Fig. 12.2; PMG 12.3). It has highly vascular dermis and because of this it appears pink. Since this area of the lip lacks glands, it remains dry and cracks in the dry weather; to prevent this, it is kept moist by saliva.
- Beneath the mucosa is a layer of connective tissue, the submucosa. Numerous serous and mucous salivary glands (minor salivary glands) are present in this layer, and the ducts of these salivary glands open into the internal surface of the lip.



**PMG 12.2** Lip—inner surface (H&E stain, X10).





**PMG 12.3** Lip—vermilion zone (H&Estain, X10).

- Underlying the submucosa is the orbicularis oris muscle (Fig. 12.2). It is a striated muscle and forms the bulk of a lip.

## TOOTH (Fig. 12.3)

- A tooth consists of two parts: crown and root. The region where the crown and the root meet is the neck.
- The part of the tooth projecting above the gum is the crown, which is covered by a cap of enamel.
- The part of the tooth covered by the gums is the root, and it is covered by cementum. Enamel and cementum meet at the neck.
- In the core of the tooth, there is a pulp cavity which is surrounded by dentin.

## ENAMEL

- Enamel is the hardest and most calcified substance in the human body. It covers the crown of the tooth.
- The main constituent of the enamel is hydroxyapatite ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ) crystals.
- Enamel is laid down by ameloblasts. These cells degenerate after the eruption of the tooth, and enamel becomes an acellular structure. Hence, enamel cannot regenerate after eruption of the tooth.

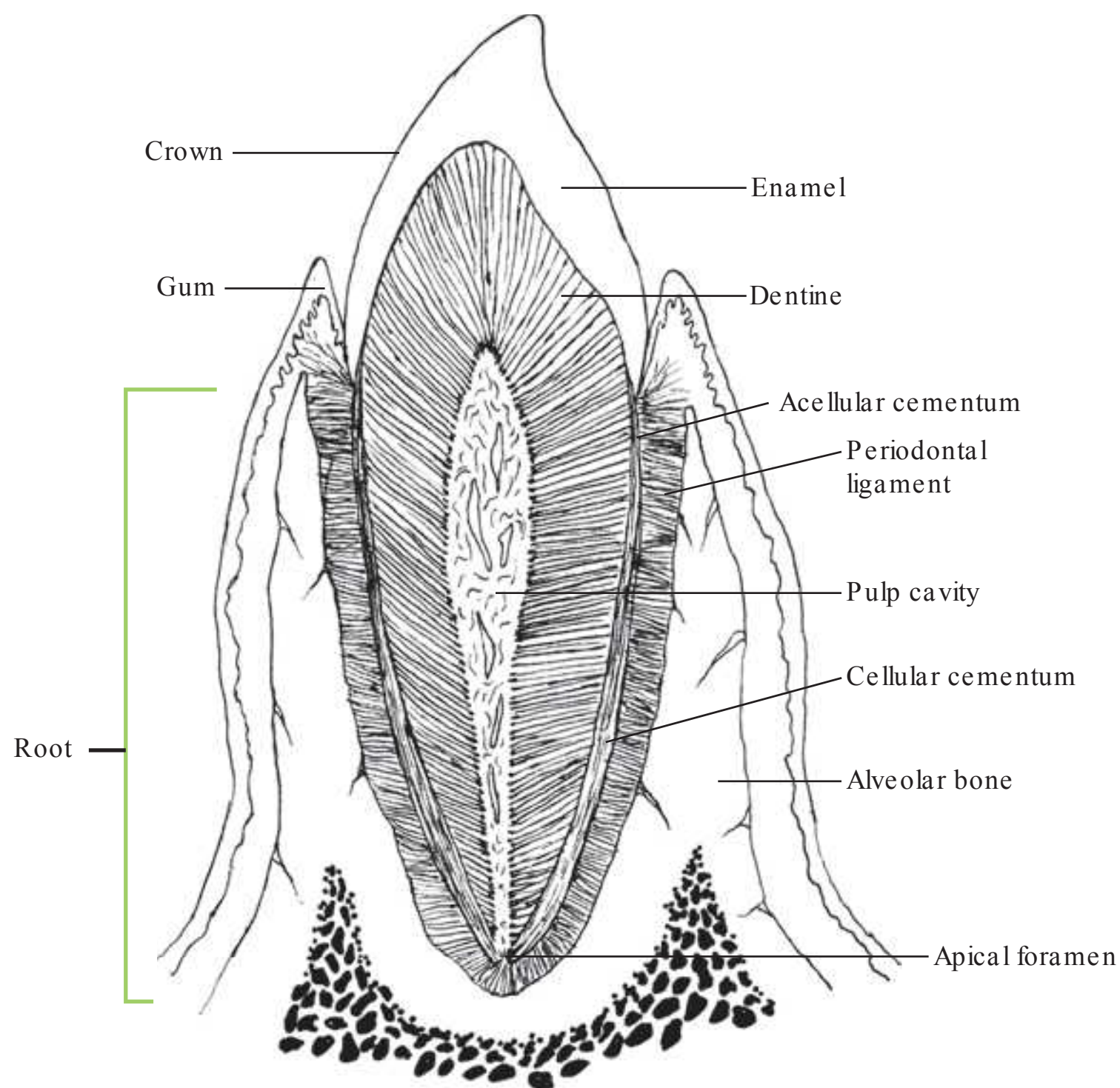
## CEMENTUM

- Cementum is a modified bone which covers the root of the tooth.
- It has acellular and cellular parts. In the upper part of the tooth (near the neck) it is acellular, and in the lower part (the cellular part) it has cementocytes.
- The organisation of cementocytes is similar to that of osteocytes in the bone; they are present in the lacuna which is surrounded by calcified matrix. Adjacent lacunae are connected to each other by canaliculi, and these canaliculi have cytoplasmic processes of cementocytes.

## PERIODONTAL LIGAMENT

- Cementum is attached to a ligament of dense connective tissue, called the periodontal ligament.
- Type I collagen fibres (Sharpey's fibres) are present in this ligament which anchors the tooth to the bony socket (alveolus) in which it sits.





**Figure 12.3** Sagittal section of a tooth.

## **DENTIN**

- Dentin is a hard, bony substance that forms the bulk of the tooth, and it surrounds the pulp cavity.
- Most of the dentin consists of inorganic substance, which is mainly the hydroxyapatite crystals. The organic components of the dentin is type I collagen.
- Dentin has minute canals radiating from the pulp cavity, and these canals are known as dentinal tubules.
- Dentin is produced by odontoblasts. These are columnar cells present around the pulp cavity. These cells have cytoplasmic processes which are present in dentinal tubules.

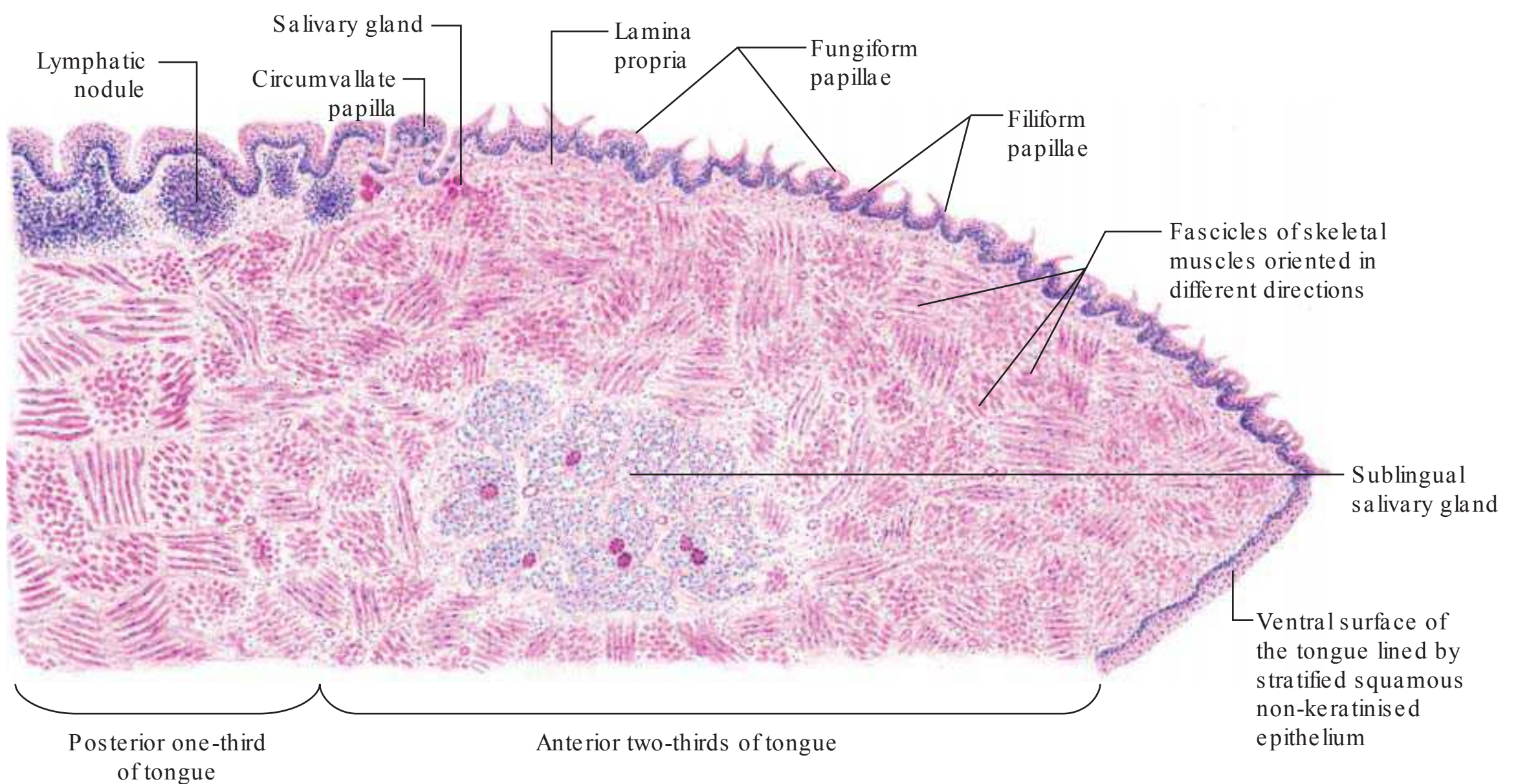
## **PULP CAVITY**

- Most of the pulp cavity is in the root; some part extends through the neck into the crown.
- It consists of loose connective tissue with many sensory nerves and blood vessels. The nerves and blood vessels pass through an opening at the apex of the root, known as apical foramen, into the pulp cavity.
- On the outer aspect, the pulp cavity is lined by odontoblasts.

## **TONGUE**

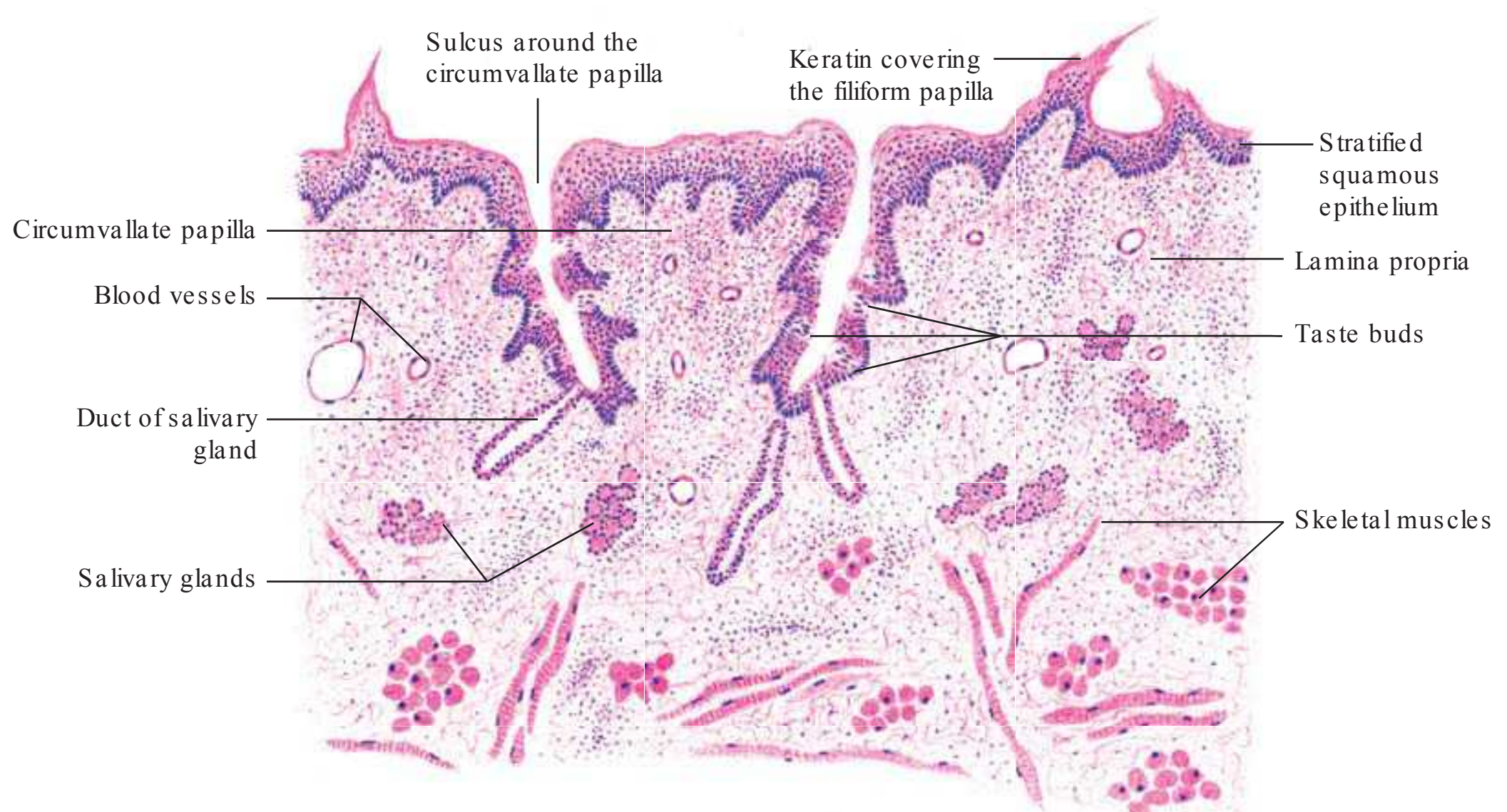
- The tongue is made up of a core of striated muscle covered by oral mucosa.
- The epithelium rests on lamina propria and the lamina propria is adherent to underlying skeletal muscles (Figs 12.4 and 12.5). There is no submucosa.





**Figure 12.4** Sagittal section of the tongue—panoramic view (H&E pencil drawing).

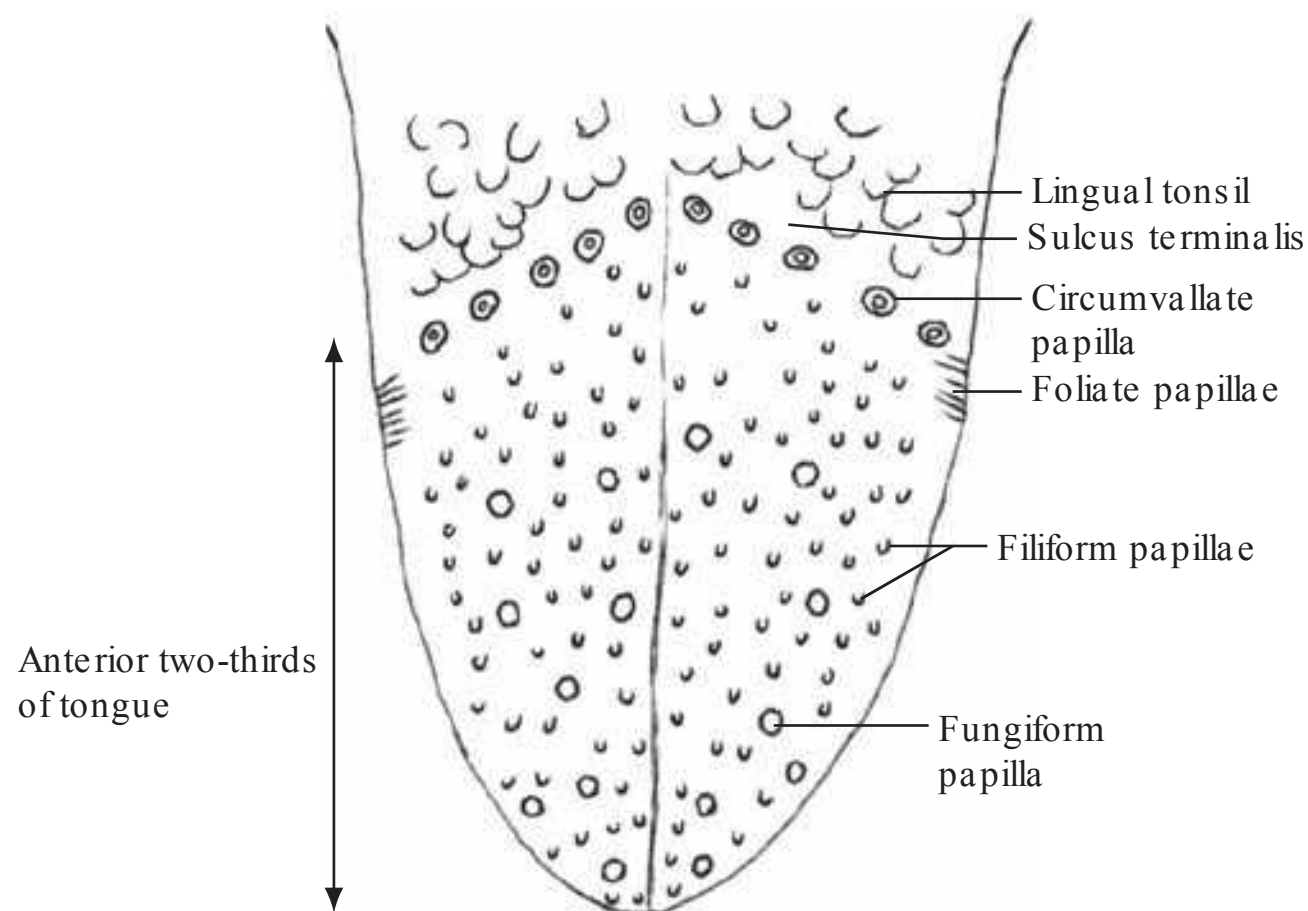
- The bundles of skeletal muscles criss-cross each other as they run in three different planes. This kind of arrangement provides the tongue with great mobility and helps in chewing, swallowing and speaking. The adjacent bundles of skeletal muscles are separated from each other by connective tissue. Numerous serous and mucous salivary glands are present in the lamina propria and in between the bundles of skeletal muscles (Fig. 12.5). These are minor salivary glands.



**Figure 12.5** Section of the tongue in low magnification (H&E pencil drawing).



- On gross appearance, the tongue has two surfaces—ventral and dorsal. The ventral surface is smooth and it is covered with oral mucosa.
- The dorsal surface of the tongue has a V-shaped groove (sulcus terminalis), which divides the tongue into anterior two-thirds and posterior one-third (Fig. 12.6). The anterior two-third part shows numerous small projections called papillae. There are four types of papillae: filiform, fungiform, foliate and circumvallate (Figs 12.4 and 12.6). The posterior one-third part has irregular surface; this is due to the presence of lymphoid tissues underneath the mucosa, called lingual tonsil (Fig. 12.4).



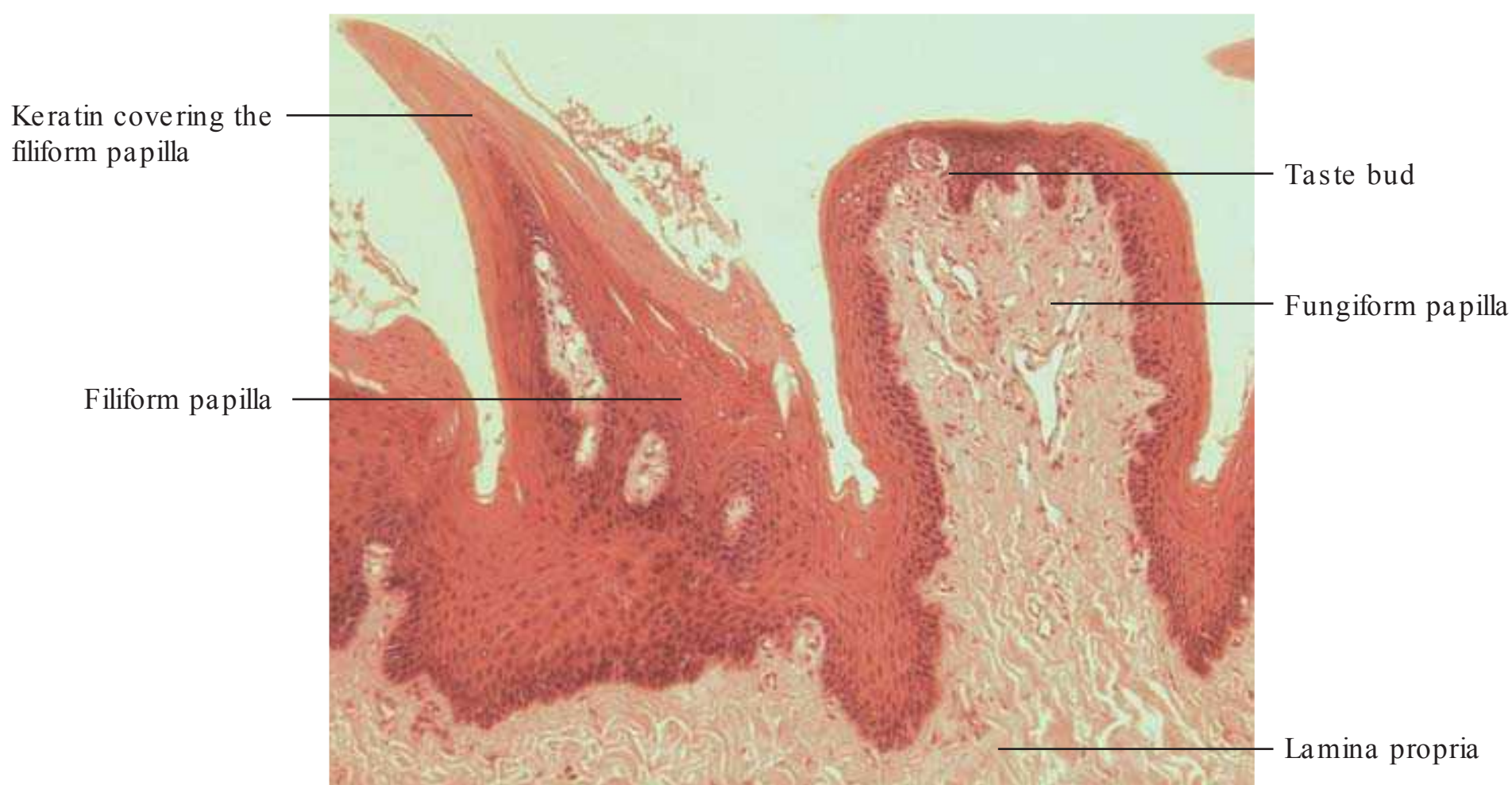
**Figure 12.6** Dorsum of the tongue.

## **PAPILLAE**

As mentioned above, papillae are of four types:

### **1. Filiform papillae**

- Filiform papillae are conical projections of lamina propria covered by keratinised epithelium (Fig. 12.5; PMG 12.4). (Note that epithelium is non-keratinised in the rest of the papillae.)
- They are the most numerous papillae and are present all over the dorsum of the tongue in the anterior two-thirds.
- They do not have taste buds; they help to hold the food.

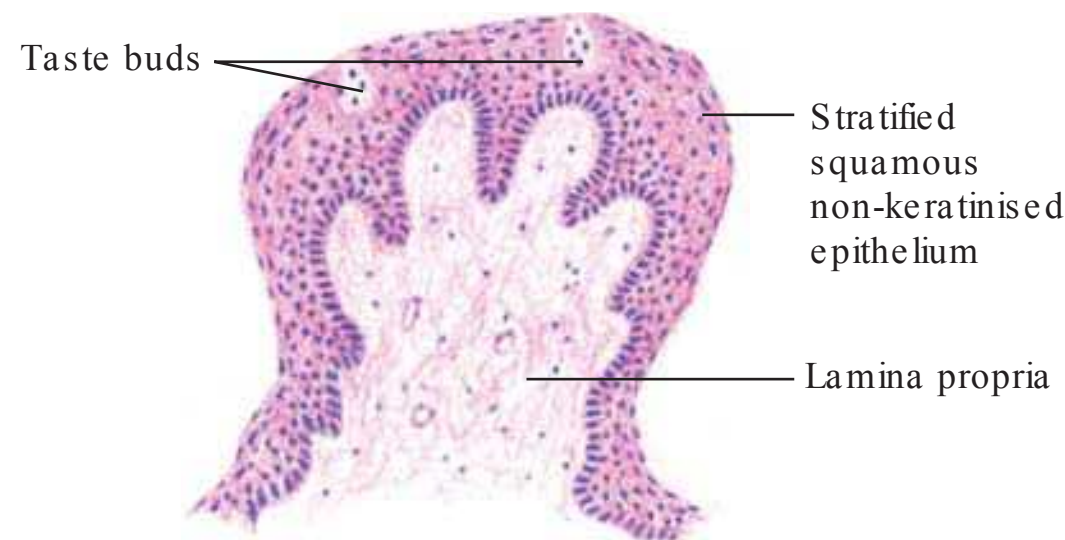


**PMG 12.4** Tongue—filiform and fungiform papillae (H&E stain, X10).



## 2. Fungiform papillae

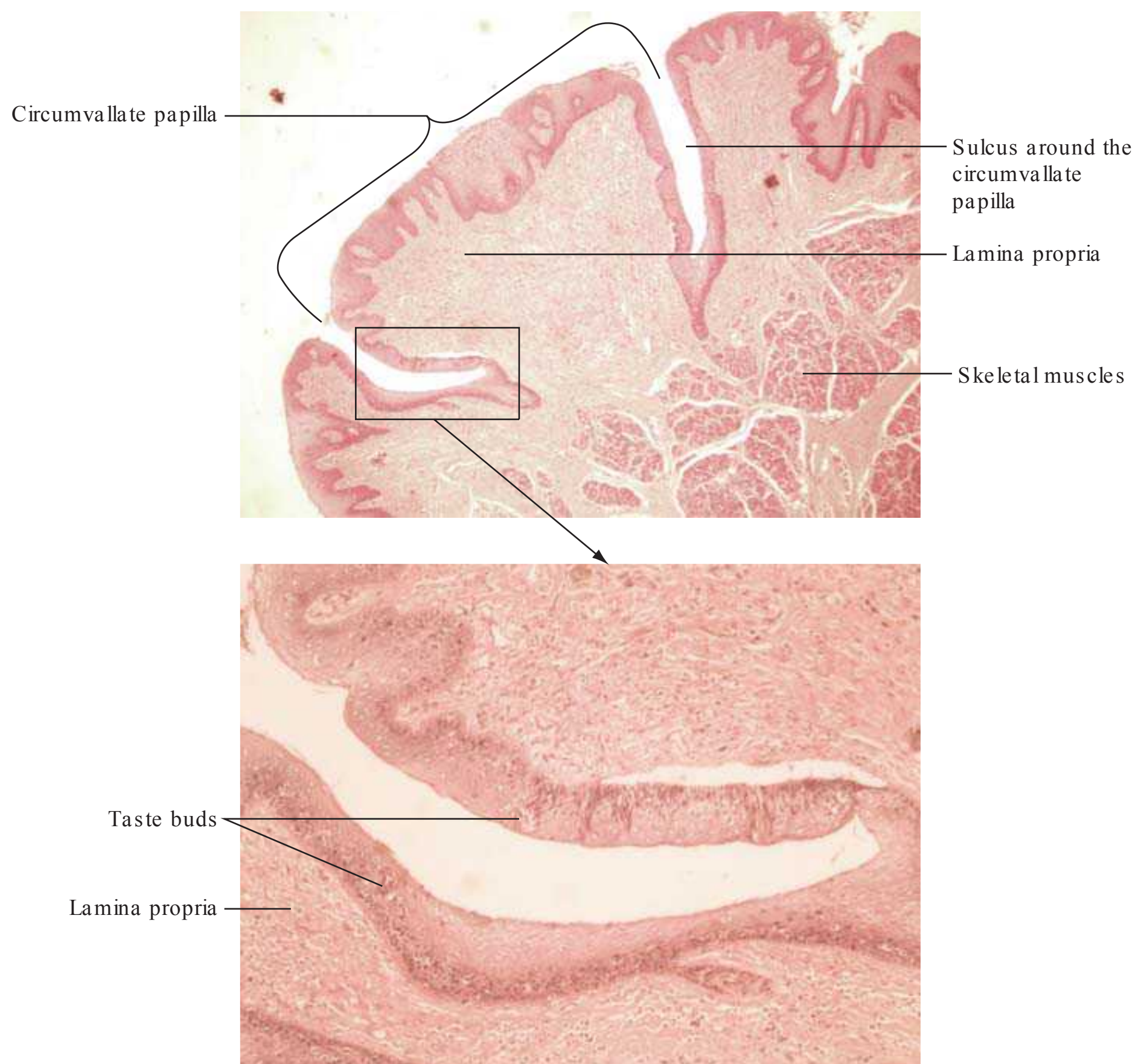
- Fungiform papillae are dispersed among filiform papillae in the anterior two-thirds of the tongue (Figs 12.4, 12.6 and 12.7; PMG 12.4).
- They are mushroom shaped and consist of a core of lamina propria which expands in the upper part.
- They have taste buds on the upper surface of the expanded part.



**Figure 12.7** Section of fungiform papilla in low magnification (H&E pencil drawing).

## 3. Circumvallate papillae

- Circumvallate papillae are the largest papillae (Figs 12.4, 12.5 and 12.6; PMG 12.5).



**PMG 12.5** Tongue—circumvallate papilla (H&Estain, X5). Inset shows enlarged view (H&Estain, X10).



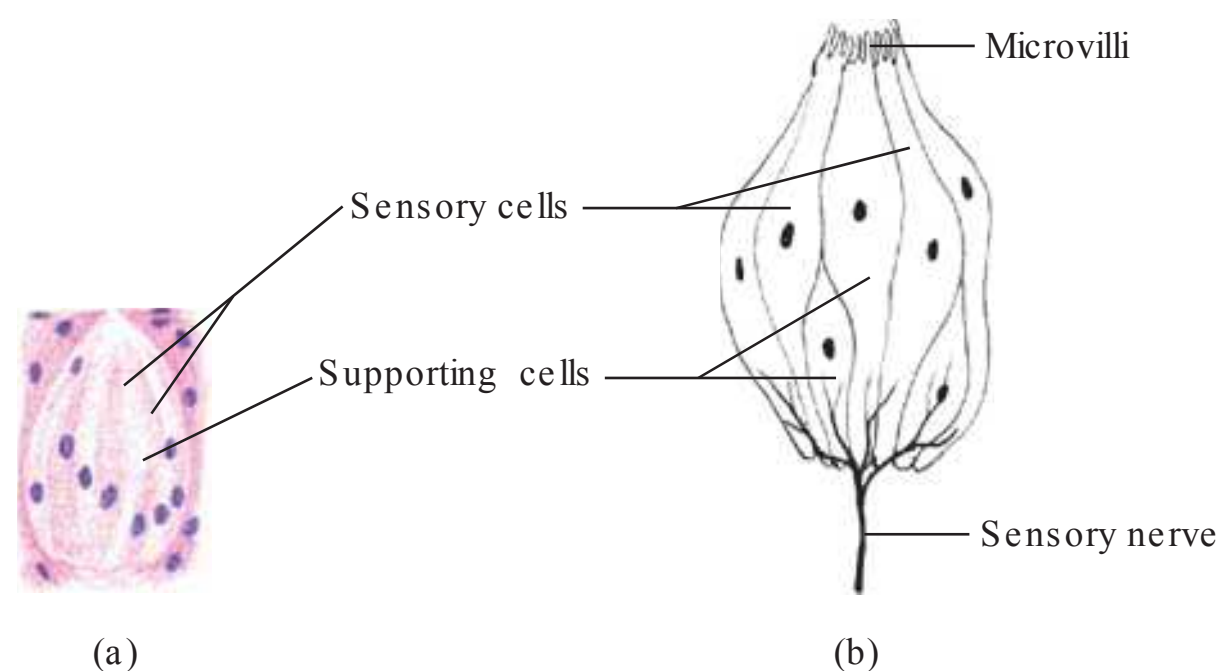
- They are 10–12 in numbers, arranged in V shape in front of and parallel to sulcus terminalis.
- Each papilla is large and circular and is surrounded by a sulcus. Walls of the sulcus have taste buds.
- Ducts of numerous serous glands open into the sulcus (Fig. 12.5). These glands are known as von Ebner's glands and their secretions make the food soluble to stimulate the taste buds.

#### 4. Foliate papillae

- Foliate papillae are poorly developed in humans.
- They are present in rows on the lateral aspect of the dorsum of the tongue in front of sulcus terminalis (Fig. 12.6).

### TASTE BUDS

- Taste buds are present on circumvallate and fungiform papillae of the tongue. A few taste buds are also seen in the lining epithelium of other parts of the oral cavity, throat and on the upper part of posterior surface of epiglottis (Fig. 15.5, page 223).
- Taste buds are oval-shaped clusters of cells. At the apical end of each taste bud, there is an opening known as taste pore which opens on the surface.
- They have three types of cells: supporting sustentacular cells, sensory receptor cells (Fig. 12.8) and basal cells. Basal cells are located in the lower part of taste buds. These are undifferentiated cells which divide and give rise to the other two types of cells.
- The apical portion of the sustentacular and sensory cells extends into the taste pore; this portion of the cells has microvilli (Fig. 12.8).
- The base of the taste bud is penetrated by a sensory nerve.
- Taste buds recognise four types of stimuli: sweet, bitter, salty and sour. Taste buds in different regions of the tongue recognise different modalities of taste stimulus—sweet at the tip, salty behind the tip, bitter at the back and sour at the lateral margins.



**Figure 12.8** Taste bud: (a) Section in high magnification (H&E pencil drawing) and (b) schematic presentation.

### CLINICAL CORRELATE

#### Squamous Cell Carcinoma

- Squamous cell carcinoma is the most common cancer of the oral cavity, caused by tobacco chewing and smoking. The common sites are lower lips, floor of the oral cavity, ventral surface of the tongue and the soft palate.

KEYPOINTS

Lips (Fig. 12.2; PMG 12.1, 12.2 and 12.3)

Surfaces	Features
Outer surface	Covered with hairy skin; dermis has sweat and sebaceous glands
Vermilion zone	Covered with modified skin which does not have glands
Inner surface	Covered by oral mucosa

- Underneath the mucosa, there is a submucosa, and numerous minor salivary glands are present in this layer.
- Underlying the submucosa is the orbicularis oris muscle which forms the bulk of a lip.

Tooth (Fig. 12.3)

- The tooth consists of mainly two parts—the crown and the root; in the core of the tooth, there is a pulp cavity surrounded by dentin.
- The pulp cavity has sensory nerves and blood vessels. It is surrounded by three calcified tissues—enamel, cementum and dentin.
- Periodontal ligament anchors the tooth to the bony socket.

	Location	Main constituent	Cells
Enamel	Covers the crown	Hydroxyapatite crystals	Ameloblasts: These cells degenerate after eruption of the tooth
Cementum (modified bone)	Covers the root of the tooth	Calcified matrix	Cementocytes: These are present in the lower part of the cementum; the upper part is acellular
Dentin	Surrounds the pulp cavity	Hydroxyapatite crystals	Odontoblasts: They are present around the pulp cavity; their cytoplasmic processes are present in dentinal tubules

Tongue (Figs 12.4, 12.5 and 12.7; PMG 12.4 and 12.5)

- The tongue is covered with oral mucosa.
- Numerous minor salivary glands are present in the lamina propria.
- Skeletal muscles form the bulk of the tongue. The bundles of skeletal muscles run in different planes.
- The dorsal surface is rough due to the presence of numerous papillae, whereas the ventral surface is smooth.
- There is no submucosa.

Papillae	Location	Taste buds
Filiform papillae	Present in the anterior two-thirds of the tongue	Absent
Fungiform papillae	Scattered among filiform papillae in the anterior two-thirds of the tongue	Present on the upper surface of the papillae
Circumvallate papillae	10–12 in numbers, located in front of sulcus terminalis	Present in the walls of the sulcus surrounding the papillae

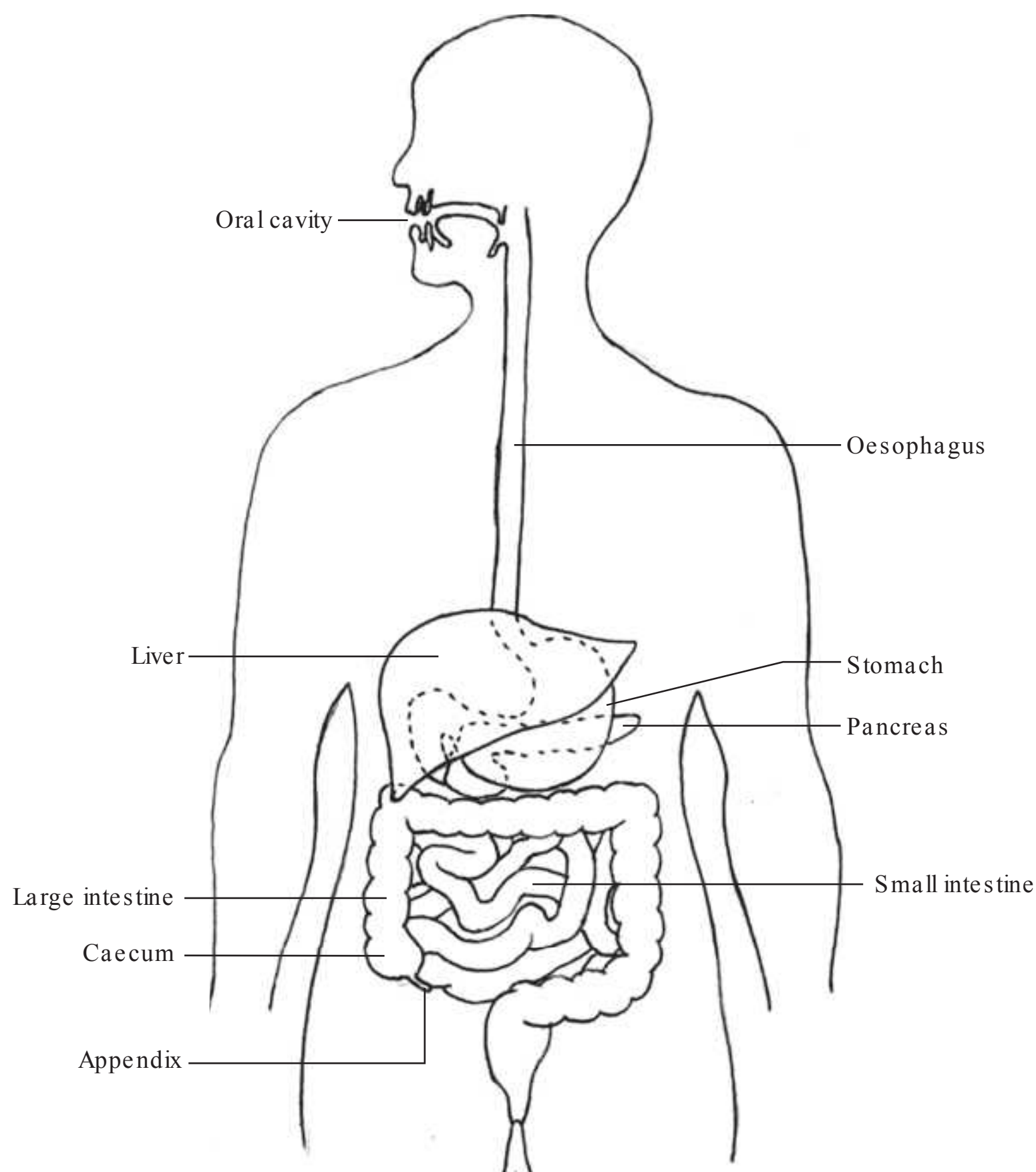


## SELF-ASSESSMENT

1. What is the lining epithelium of the oral cavity?
2. What is vermillion zone?
3. What is the composition of the pulp cavity of the tooth?
4. What is periodontal ligament?
5. What are the different types of papillae in the tongue? Give their location on the tongue.
6. Describe the structure of a taste bud.

# Gastrointestinal Tract

- The gastrointestinal tract (GIT) is a long muscular tube. It begins with the oral cavity and ends in the anus.
- The parts of the GIT are the oral cavity, the pharynx, the oesophagus, the stomach, the small intestine and the large intestine (Fig. 13.1).
- The main function of the GIT is digestion. Several glands help in bringing about this function. These glands may be present either within the tract or outside it, but all of them open inside the tract.
- Different parts of the tract are specialised to perform different functions, and hence structural modifications are seen in various parts of the GIT.



**Figure 13.1** The gastrointestinal tract.



## GENERAL MICROSCOPIC FEATURES OF GIT

The GIT consists of four layers (from inside to outside): mucosa, submucosa, muscularis externa and serosa or adventitia (Fig. 13.2).

### MUCOSA

Mucosa consists of lining epithelium, lamina propria and muscularis mucosa.

#### Epithelium (Fig. 13.2)

- The epithelium performs three functions: protection, absorption and secretion.
- It gets modified according to the function it has to perform.

#### Lamina Propria (Fig. 13.2)

- The lamina propria supports the overlying epithelium.
- It is composed of loose connective tissue.
- It is rich in blood supply and lymphatics; the digested food enters the blood in this layer.
- It may also contain glands and lymphoid follicles.

#### Muscularis Mucosa (Fig. 13.2)

- The muscularis mucosa separates mucosa from submucosa.
- It consists of inner circular and outer longitudinal layers of smooth muscles.
- It produces localised movements of the mucous membrane.

### SUBMUCOSA

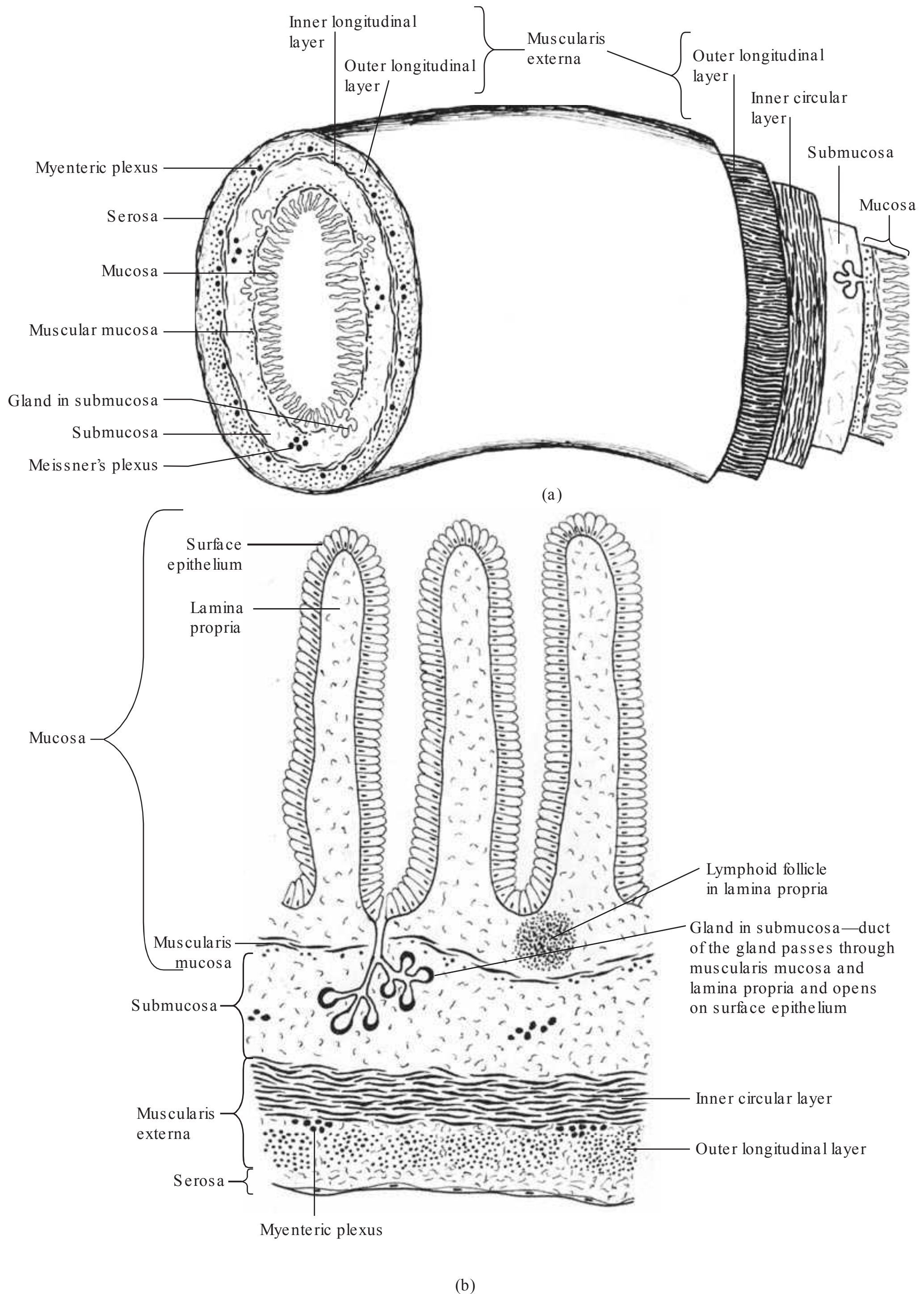
- Submucosa is present between mucosa and muscularis externa.
- It consists of loose connective tissue (Fig. 13.2).
- Apart from blood vessels and lymphatics, it also has a plexus of autonomic nerves, the submucosal plexus, also called Meissner's plexus.
- It may also contain glands.

### MUSCULARIS EXTERNA

- It consists of two layers of smooth muscle: the inner circular and the outer longitudinal layers.
- In between these two layers of smooth muscles lies a plexus of autonomic nerves called Auerbach's or myenteric plexus (Fig. 13.2).
- Contraction of this layer propels the food contents.

### SEROSA AND ADVENTITIA

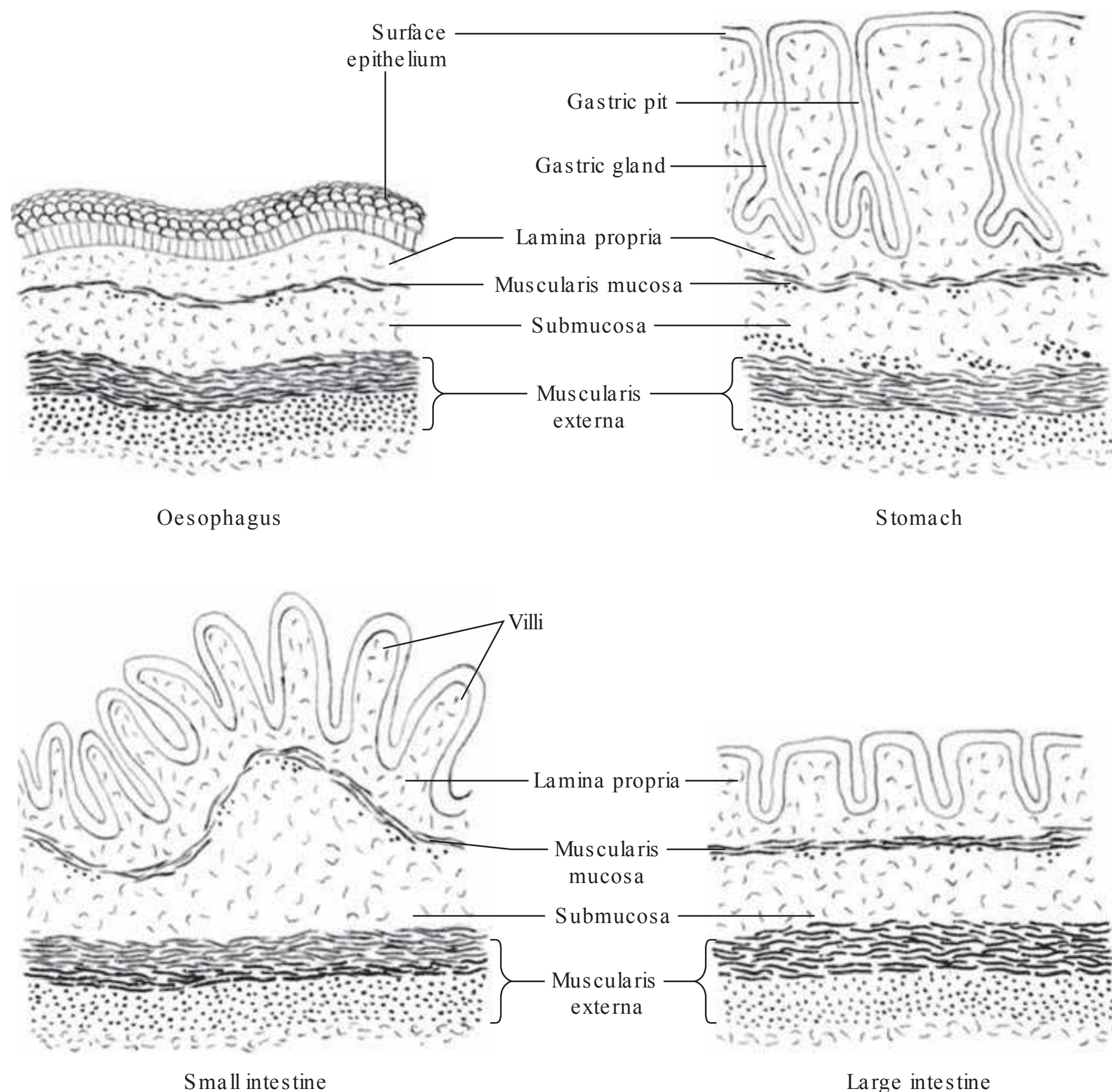
- The outermost layer of GIT is either serosa or adventitia.
- The adventitia consists of loose connective tissue which is continuous with the same type of tissues of neighbouring organs.
- In the abdominal part of the GIT, the adventitia is covered by simple squamous epithelium (mesothelium); the adventitia and the mesothelium together are called serosa (Fig. 13.2).
- Parts of the GIT covered with peritoneum have serosa, whereas the retroperitoneal parts of the GIT have serosa on the anterior wall and adventitia on the posterior wall (see Fig. 13.20).



**Figure 13.2** (a) General organisation of the gastrointestinal tract (GIT) which consists of four layers (from inside to outside): mucosa, submucosa, muscularis externa and serosa or adventitia. The left end of the figure shows the transverse section of the GIT. At the right end, three-dimensional organisation of four layers can be seen. (b) An enlarged view of the organisation of four layers of the GIT in transverse section.



- The basic structures of the oesophagus, stomach, small intestine and large intestine are shown in Figure 13.3. It is the mucosa in which changes are seen in different parts of the GIT; the other layers remain almost the same (Fig. 13.3).



**Figure 13.3** Regional differences in the mucosa of different parts of the gastrointestinal tract.

## OESOPHAGUS

The oesophagus is an approximately 25-cm-long muscular tube which begins at the level of cricoid cartilage. Proximally, it is continuous with oropharynx, and distally, it passes through the posterior mediastinum, penetrates the diaphragm and opens into the cardiac end of the stomach.

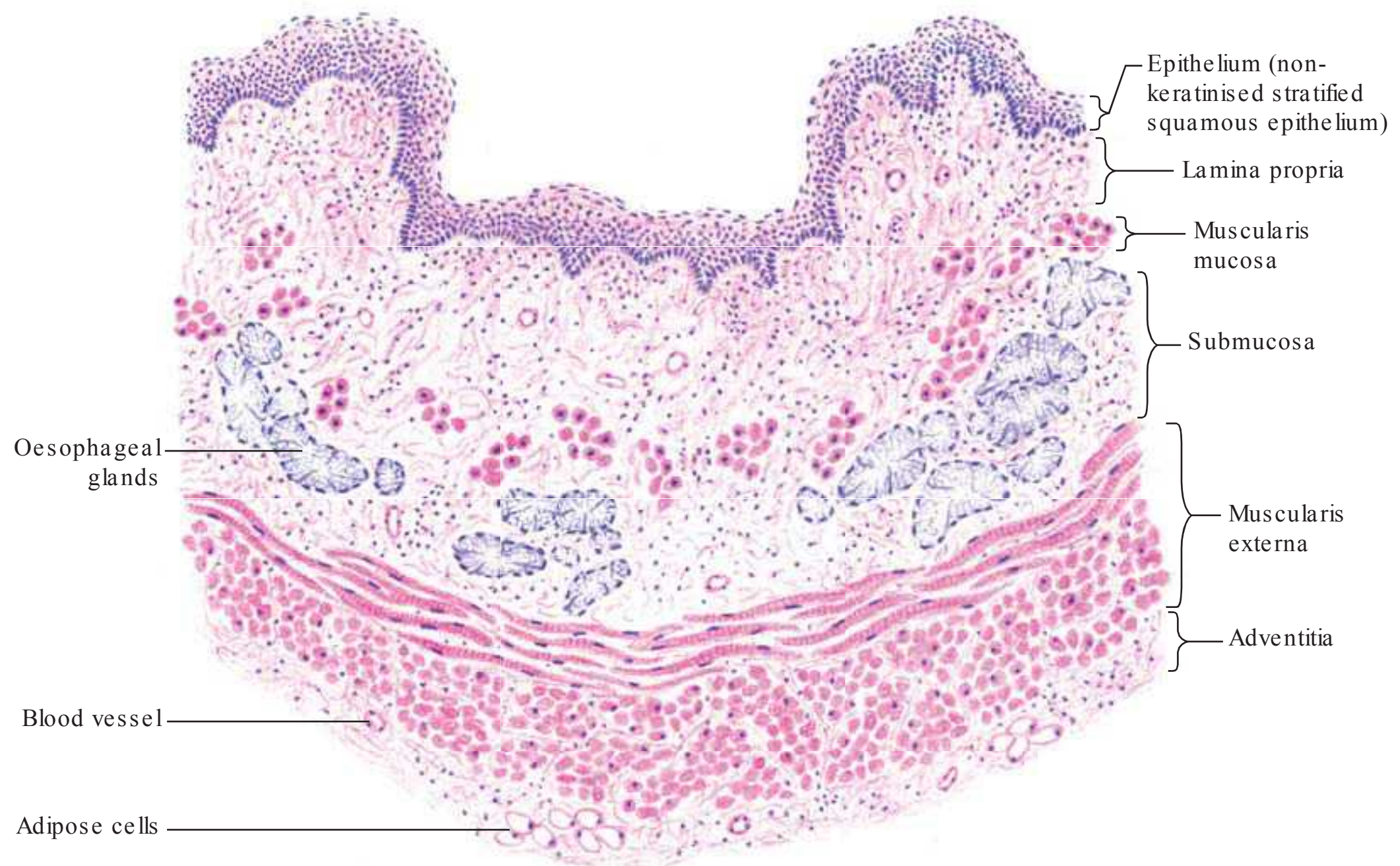
### MICROSCOPIC FEATURES

The oesophagus consists of four layers as discussed previously in the general structure of the GIT. The salient features of these layers are described as follows:

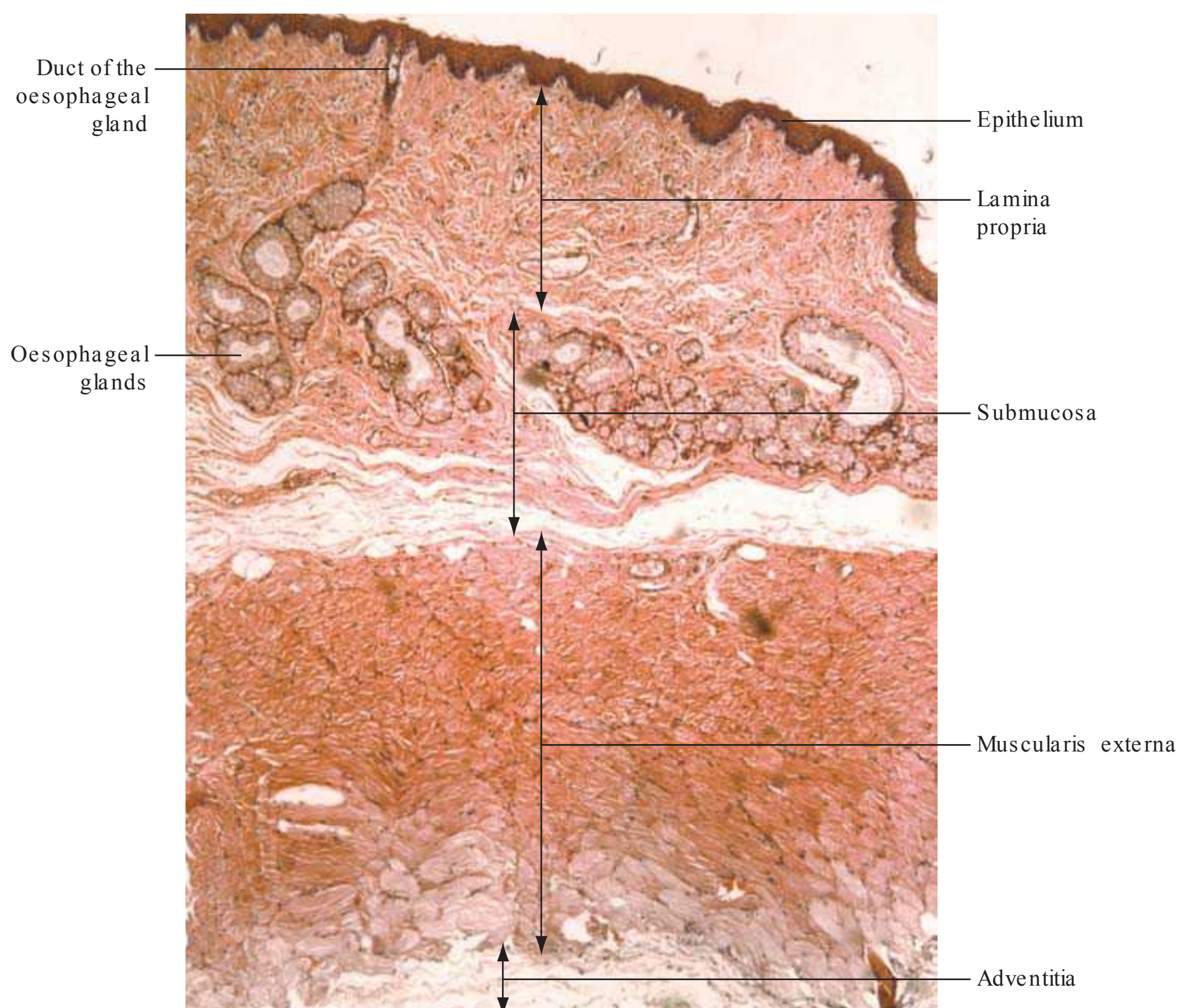
#### 1. Mucosa

- Epithelium is non-keratinised stratified squamous epithelium, which is protective in function (Fig. 13.4; PMG 13.1).
- Lamina propria has a few lymphoid follicles.
- A thin layer of muscularis mucosa is present.





**Figure 13.4** Section of the upper one-third of oesophagus in low magnification (H&E pencil drawing).



**PMG 13.1** Oesophagus (H&E stain, X10).



## 2. Submucosa

- Submucosa has mucous glands called oesophageal glands which secrete mucus (Fig. 13.4; PMG 13.1). Mucus acts as lubricant. The other components of the submucosa are the same as described in ‘General Microscopic Features of GIT’.

## 3. Muscularis externa

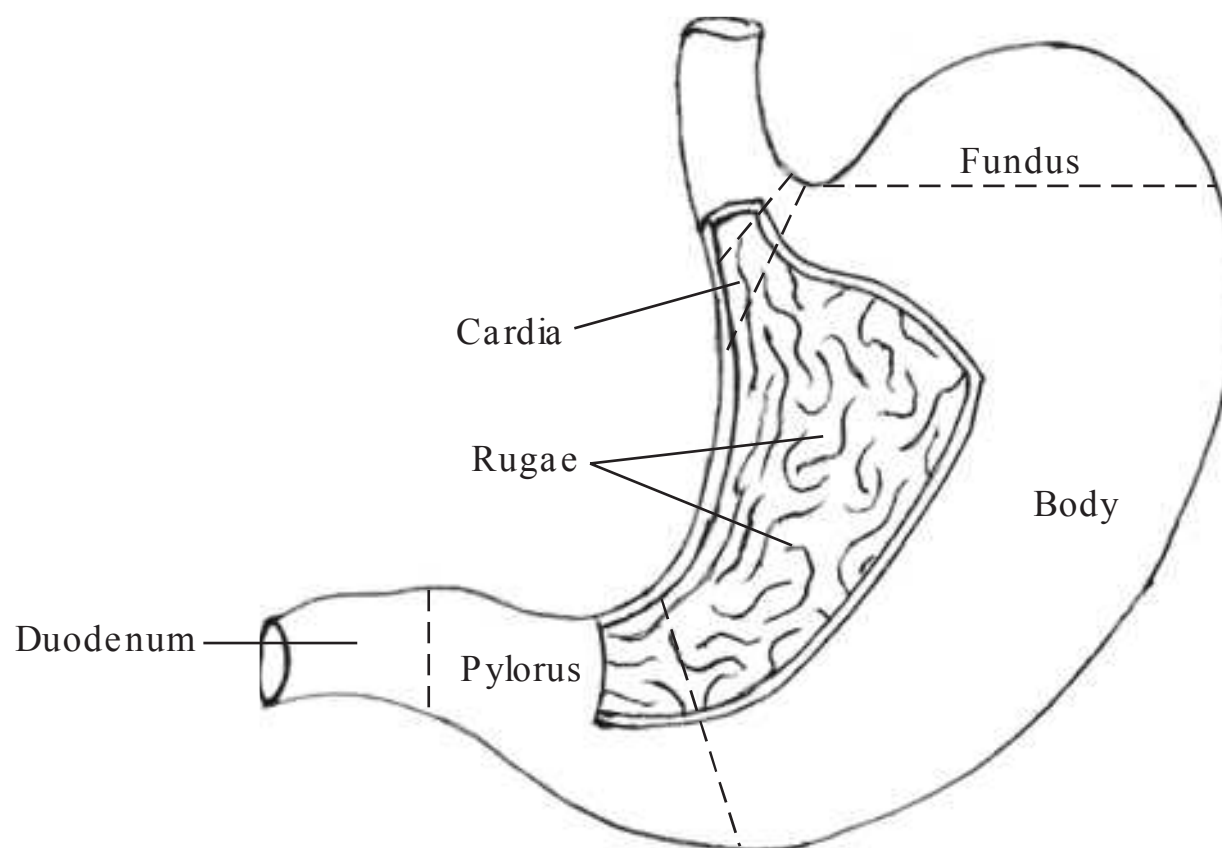
- Muscularis externa is thick and differs in different regions of the oesophagus—in the upper one-third it consists of skeletal muscle, in the middle one-third it has both skeletal and smooth muscles and in the lower one-third it has only smooth muscle.

## 4. Fourth layer

- The fourth layer in thoracic part of the oesophagus is adventitia, and in abdominal part it is serosa.

# STOMACH

- The stomach is the expanded part of the GIT. The food passes through the oesophagus and enters the stomach where it is converted into a thick paste known as chyme.
- The stomach is divided into four regions: cardia, fundus, body and pylorus (Fig. 13.5).



**Figure 13.5** Parts of stomach.

## MICROSCOPIC FEATURES

### 1. Mucosa

- The mucosa of an empty stomach shows numerous temporary folds called rugae (singular: ruga). These folds disappear when the stomach is distended (Fig. 13.6; PMG 13.2).
- The mucosa of fundus and body of the stomach differs from the mucosa of pylorus. This has been described subsequently.

### 2. Muscularis mucosa and submucosa

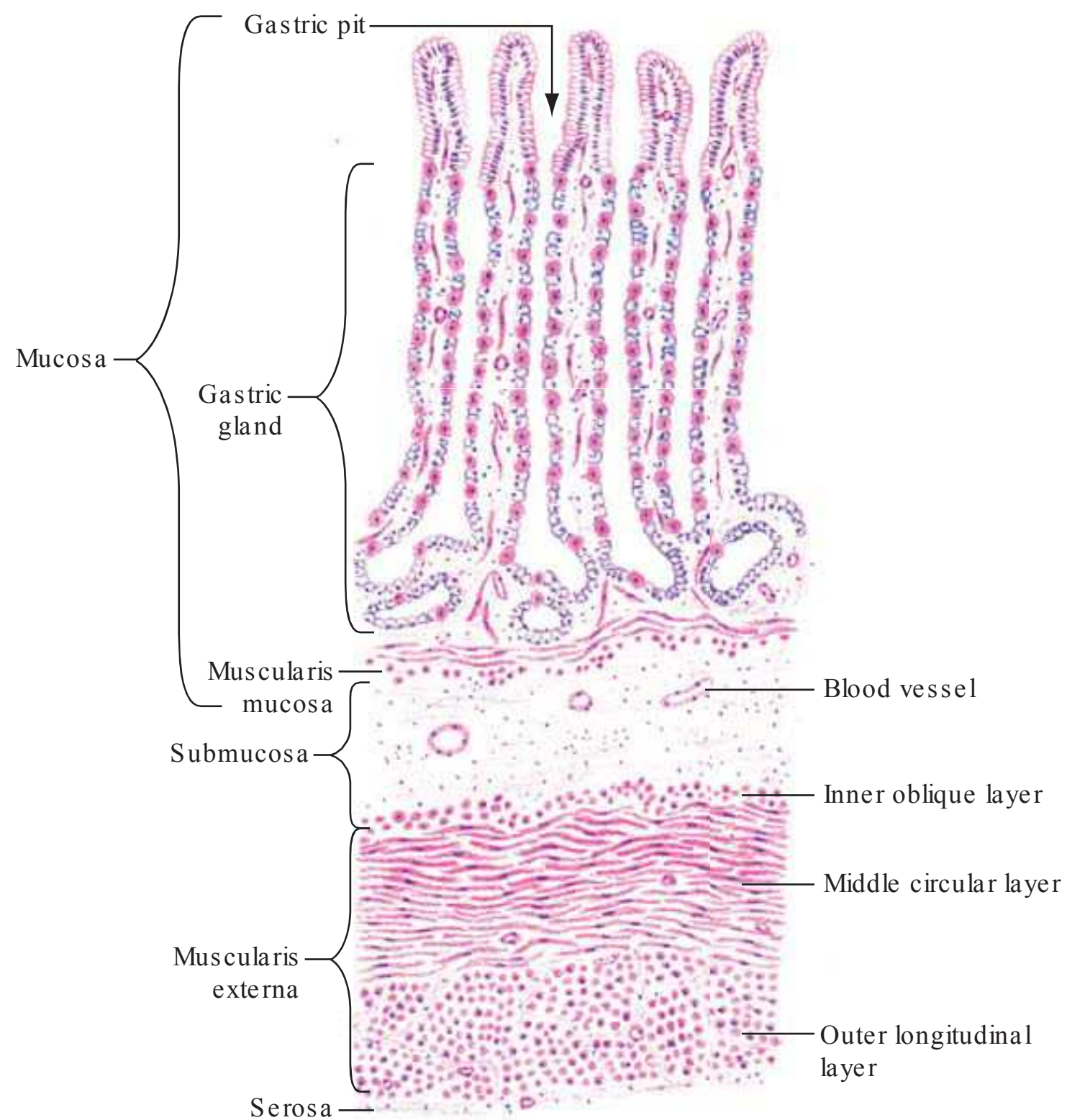
- These layers are the same as described under the section ‘General Microscopic Features of GIT’.

### 3. Muscularis externa

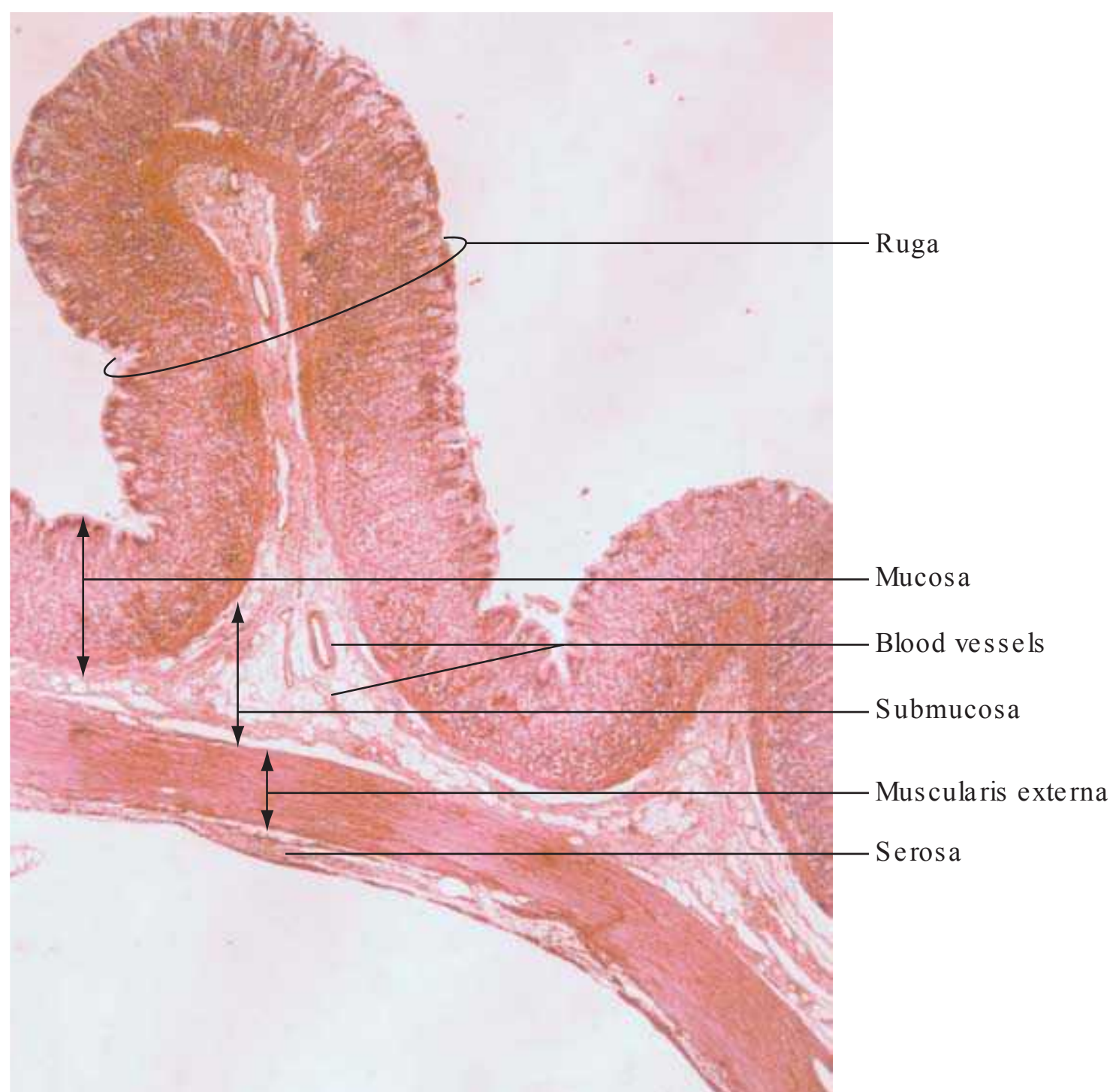
- It consists of three layers: inner oblique, middle circular and outer longitudinal layers of smooth muscles.
- In the pylorus of the stomach, the middle circular layer becomes thick to form pyloric sphincter.

### 4. Serosa

- This is the fourth layer.



**Figure 13.6** Section of stomach—fundus and body regions in low magnification (H&E pencil drawing).



**PMG 13.2** Section of the stomach (H&E stain, X2.5).



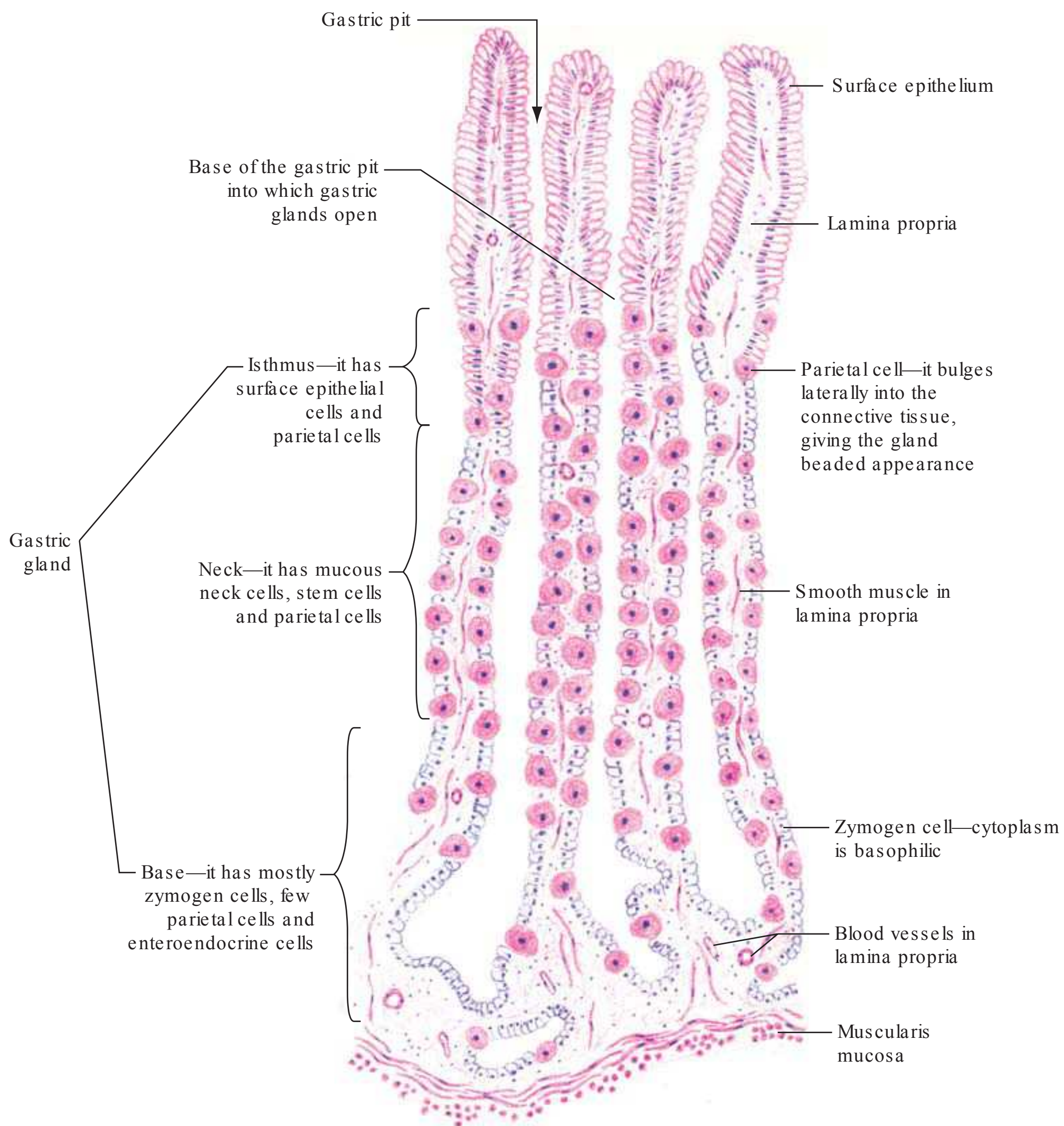
## Mucosa of the Body and Fundus of the Stomach (Figs 13.6 and 13.7; PMG 13.3)

### 1. Epithelium

- It is simple columnar epithelium.
- These epithelial cells secrete mucus. A mucous film is formed covering the gastric mucosa and this protects the mucosa of the stomach from acidic gastric juice.
- The surface epithelium invaginates into the lamina propria to form a gastric pit. Gastric glands open into the bases of gastric pits.

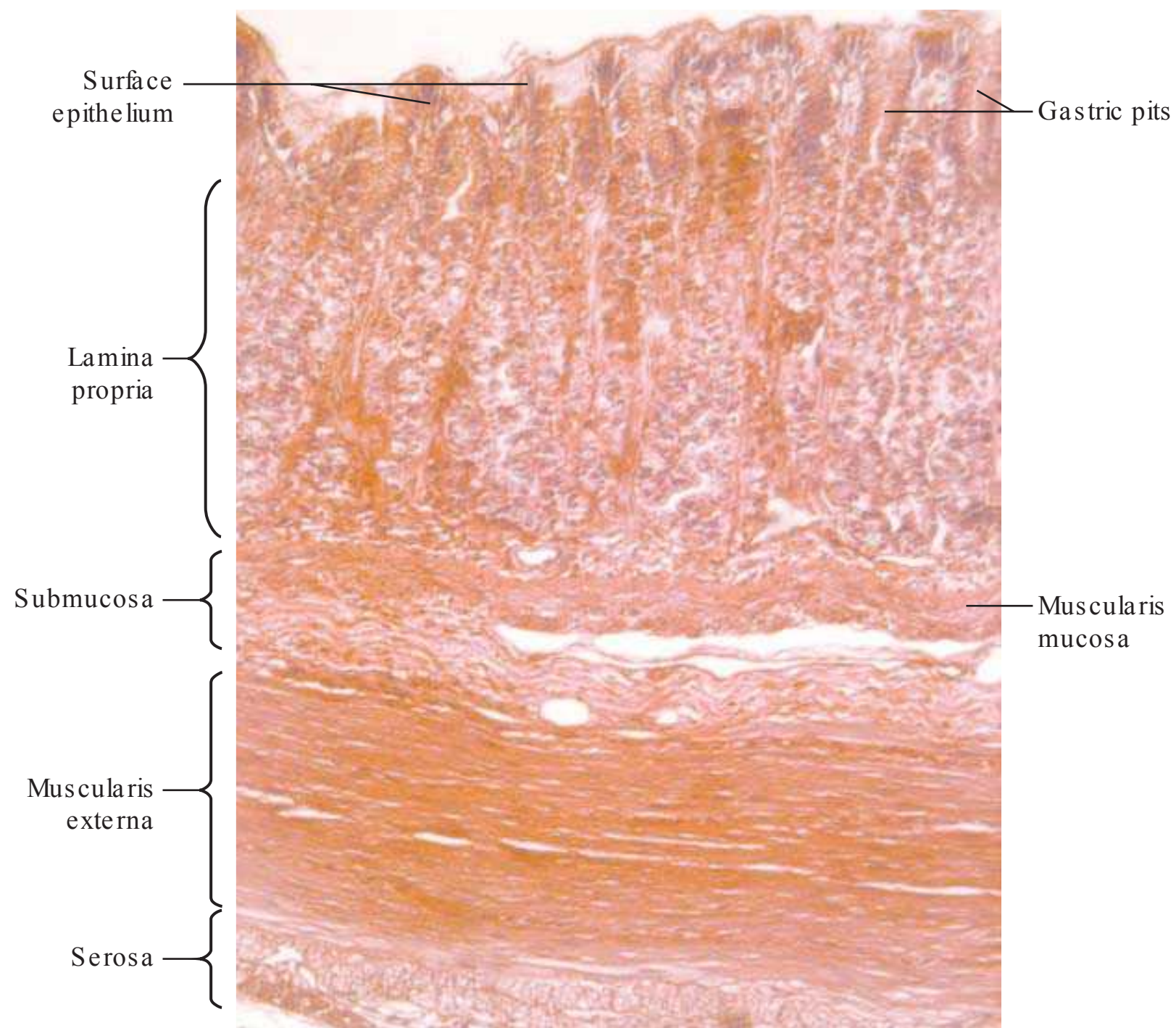
### 2. Lamina propria

- Apart from the loose connective tissue, lymphoid tissue, blood vessels and lymphatics, the lamina propria has gastric glands and some smooth muscles extending from the muscularis mucosa.

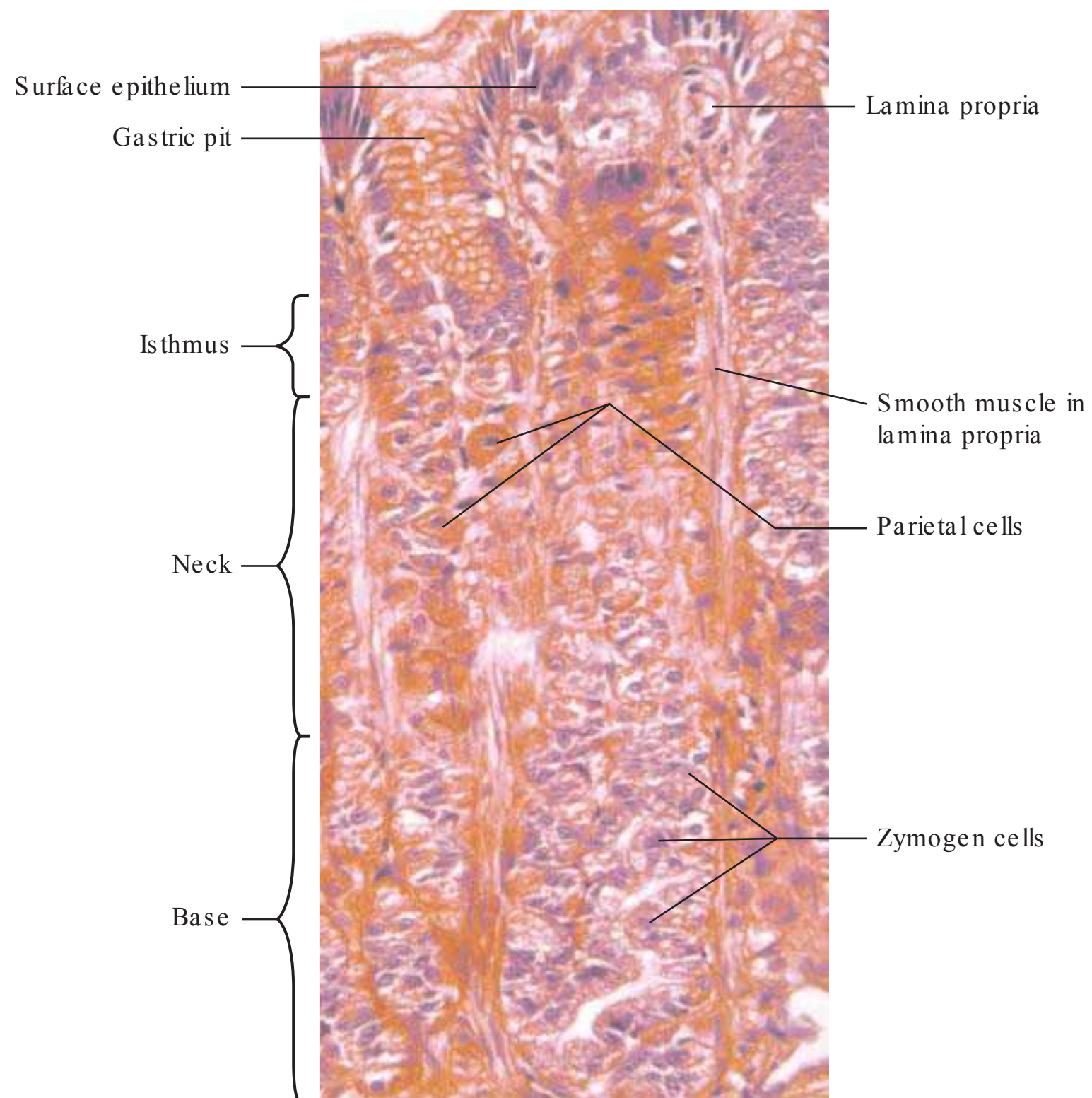


**Figure 13.7** Section of mucosa of the stomach—fundus and body regions—in high magnification (H&E pencil drawing).





(a)



(b)

**PMG 13.3** Stomach—fundus: (a) X10 and (b) X20 (H&E stain).

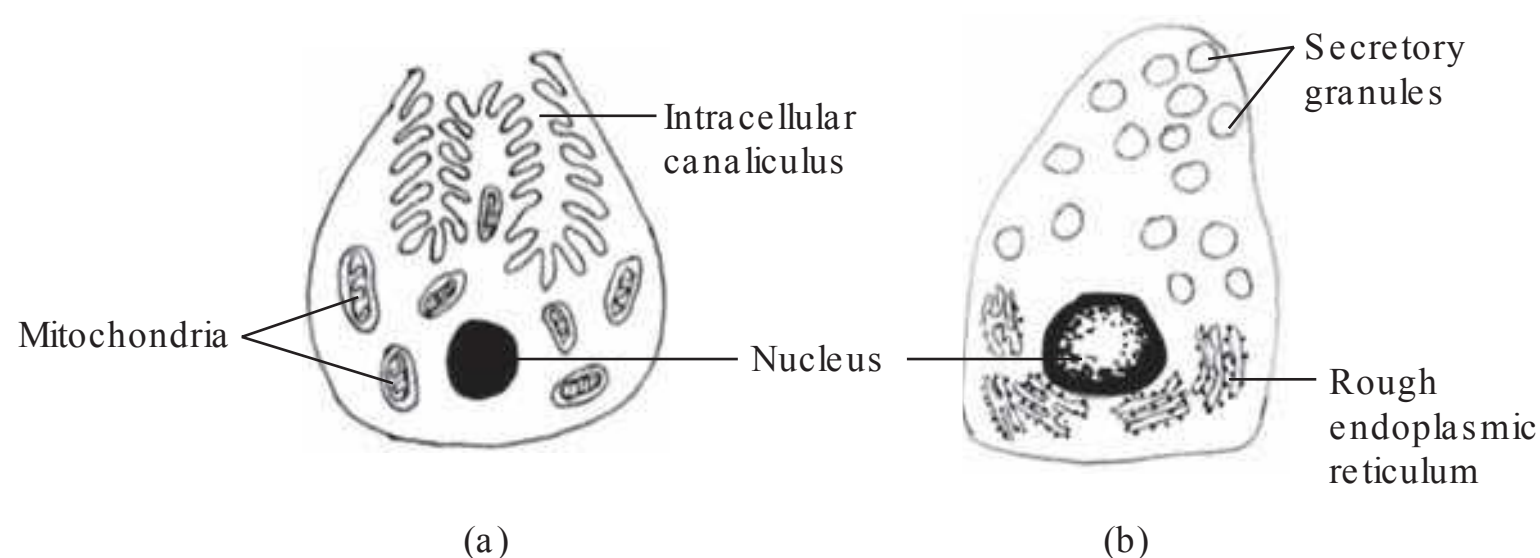


### 3. Gastric glands

- Gastric glands are present in the lamina propria and they open into the bases of gastric pits (it should be noted that the gastric pit is not a part of gastric glands). The ratio between the depth of the gastric pit and the gastric gland is 1:3 (shorter pits and longer glands).
- They are branched simple tubular glands.
- These glands have three parts: the upper part of the gland which opens into the gastric pit is called isthmus, below the isthmus is the neck and the lower part of the gland which is coiled is the base.
- Isthmus consists of surface epithelial cells and parietal cells. The neck consists of mucous neck cells, stem cells and parietal cells. The base consists of mostly zymogen cells; it also has some parietal cells and enteroendocrine cells.
- Cells of the gastric glands in the body and fundus of the stomach are as follows:
  - Parietal cells: They are also called oxyntic cells. They are present in all the regions of the gland with very few present at the base. They secrete gastric acid. They also secrete intrinsic factor, which is required for the absorption of vitamin B12.  
These cells are triangular and bulge laterally into the connective tissue, giving the gland a beaded appearance. Cytoplasm is eosinophilic due to the presence of numerous mitochondria. The apex of the cell has intracellular canaliculus, inside which there are numerous microvilli (Fig. 13.8a).
  - Stem cells: Stem cells can get differentiated into other types of cells present in gastric glands. They are present in the neck region of the gland.
  - Mucous neck cells: They are present in between the parietal cells of the neck region of the gland and secrete mucus. The nucleus of these cells is basal in location and is round.
  - Zymogen cells: They are also called chief cells (Fig. 13.7; PMG 13.3b). They are present in the base of the glands and secrete gastric enzymes (pepsinogen, rennin and gastric lipase). These cells have large nuclei located at the base of the cells (Fig. 13.8b). Cytoplasm is basophilic due to the presence of numerous rough endoplasmic reticulum.
  - Enteroendocrine cells: They are mainly present in the base of the glands and secrete serotonin.

### 4. Muscularis mucosa

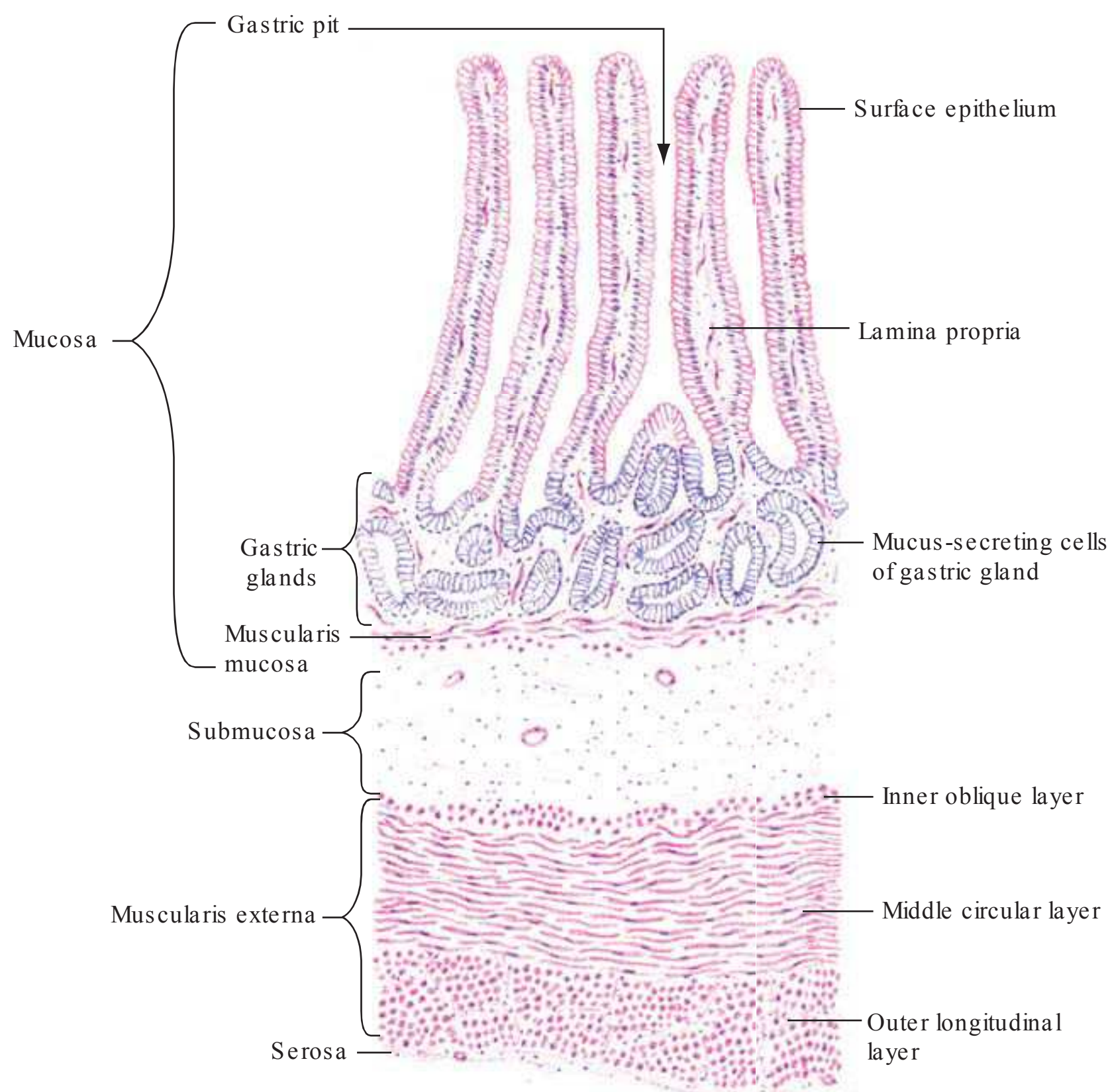
- A thin layer of muscularis mucosa is present.



**Figure 13.8** (a) Parietal and (b) zymogen cells.

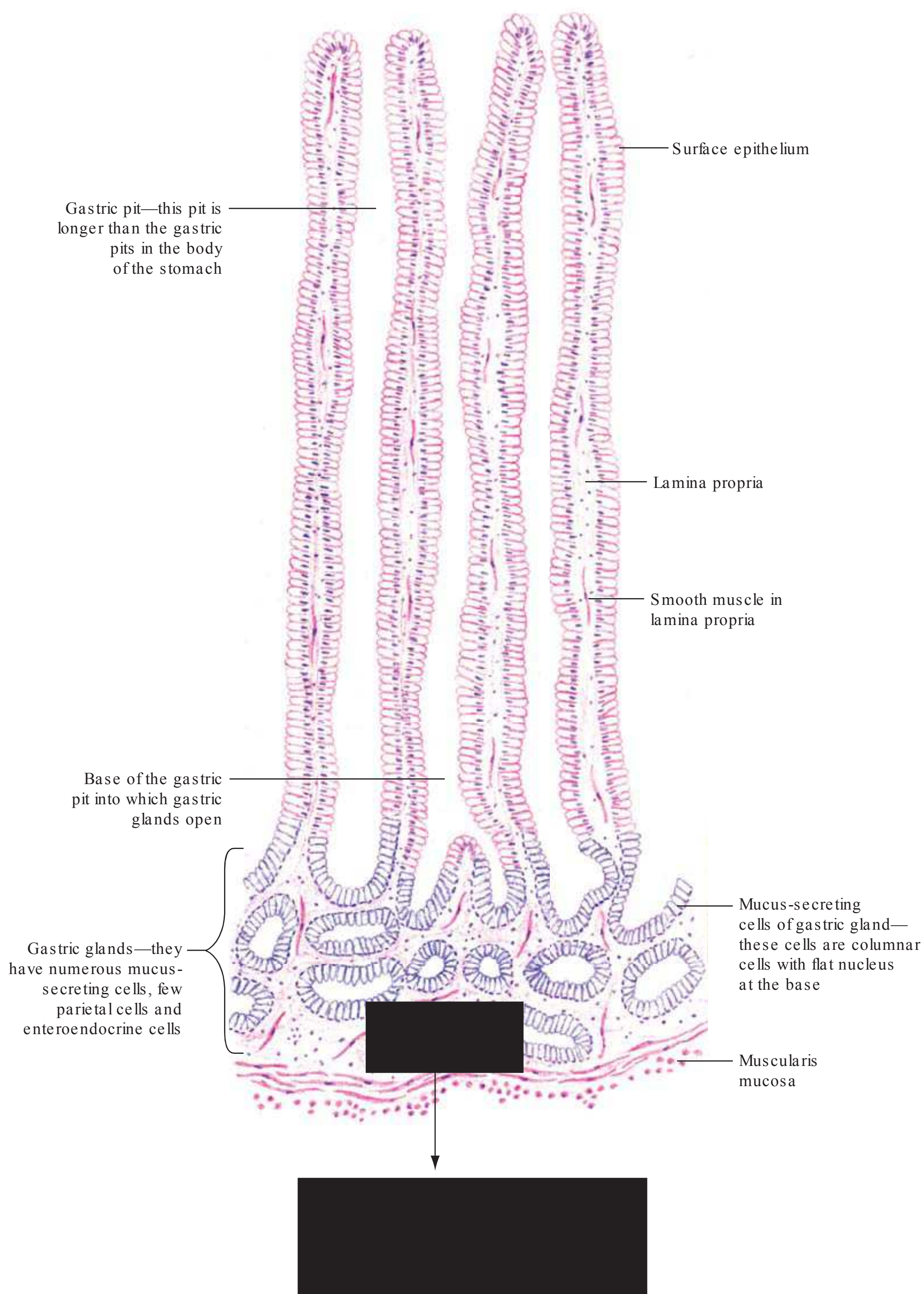
## Mucosa of Pylorus

- The mucosa of pylorus is similar to that of fundus and body in many respects. The points of differentiation are mentioned below:
  - (a) The gastric pits are longer than the gastric pits in the body of the stomach.
  - (b) The ratio between the depth of the gastric pit and the gastric gland is 3:1 (longer pits and shorter glands) (Figs 13.9 and 13.10; PMG 13.4).
  - (c) The bases of the glands are more coiled than the glands in the body of the stomach.
- The cells of the gastric glands in the pylorus of the stomach are mucus-secreting cells, parietal cells and enteroendocrine cells. It should be noted that no zymogen cells are present in the pyloric region.
  - (a) Mucus-secreting cells: Most of the cells in the gastric glands of this region are mucus-secreting cells, which are columnar cells with flat nucleus at the base (Figs 13.9 and 13.10).
  - (b) Parietal cells and enteroendocrine cells: These cells are very few in number. The enteroendocrine cells (G cells) secrete gastrin (hormone).



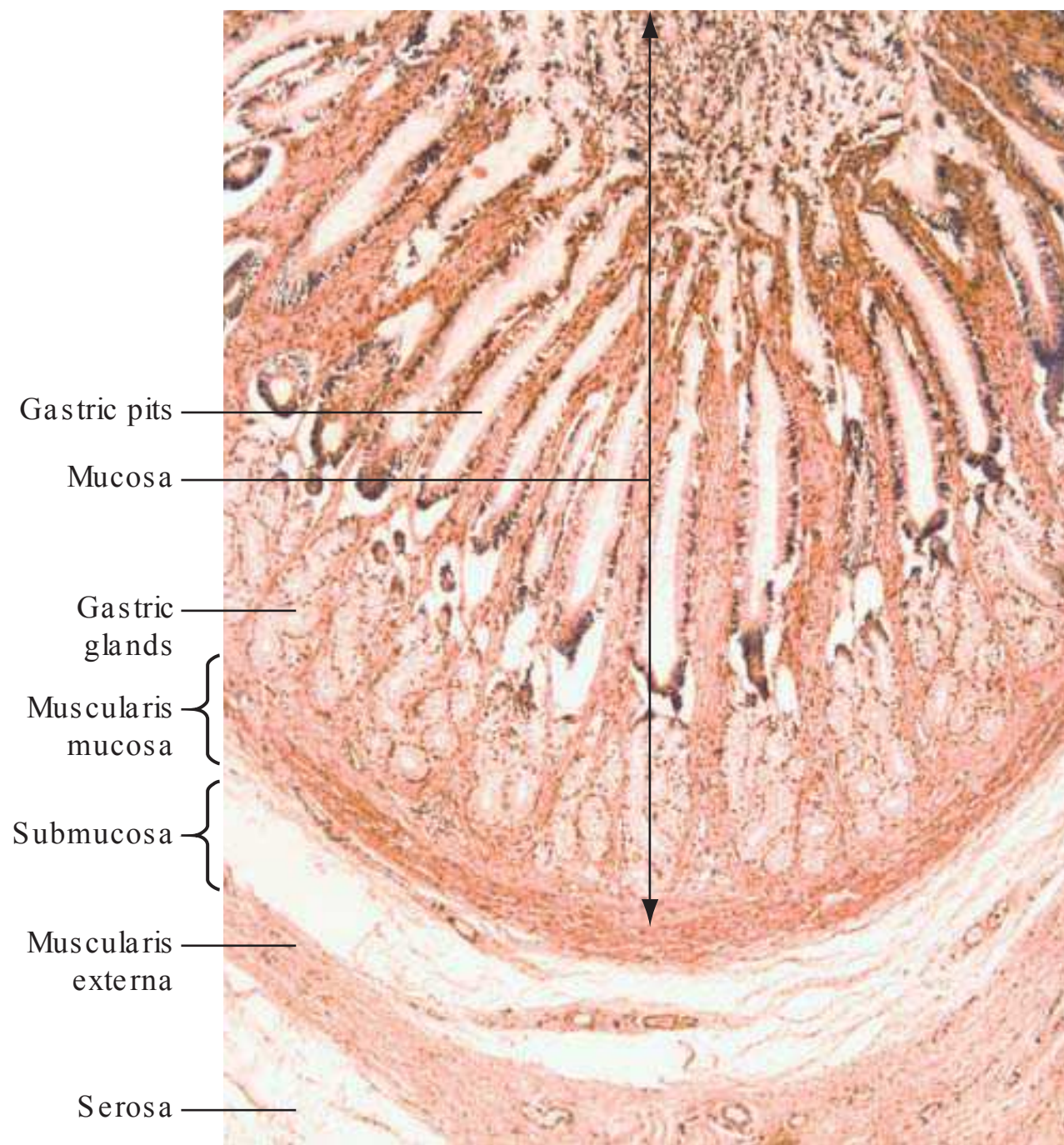
**Figure 13.9** Section of the stomach—pyloric region in low magnification (H&E pencil drawing).



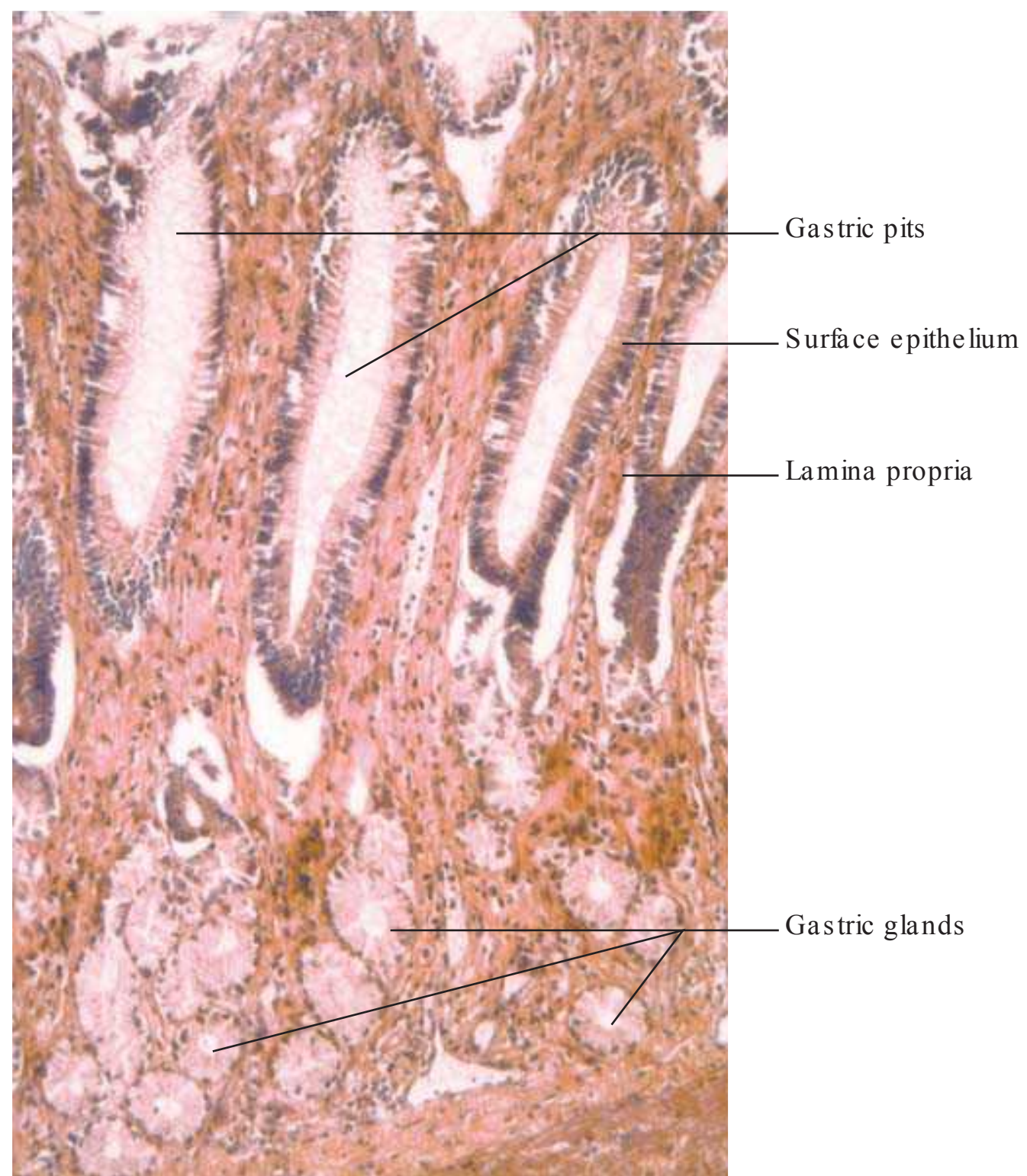


**Figure 13.10** Section of the stomach—pyloric region in high magnification. Inset shows a further enlarged view of gastric glands. (H&E pencil drawing)





(a)

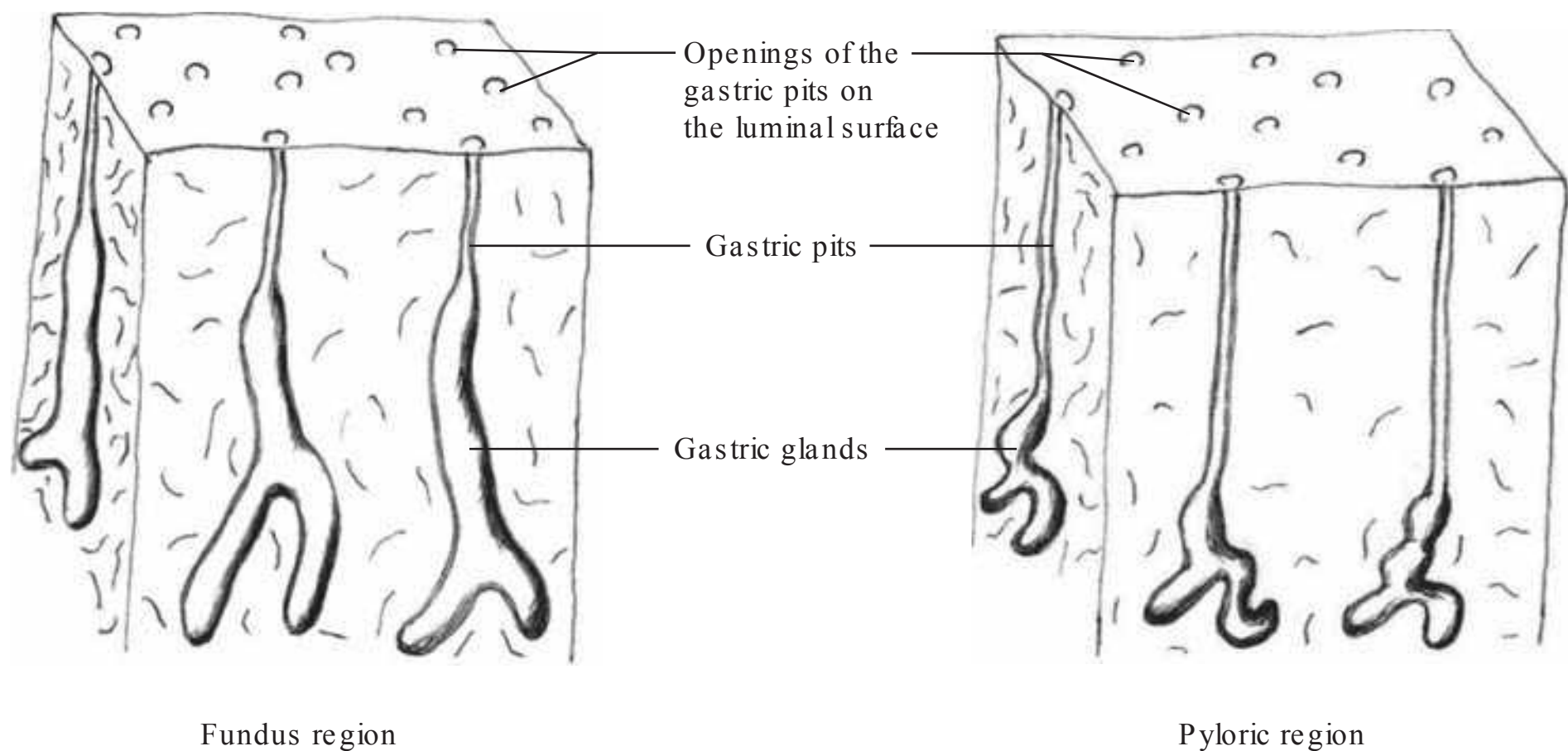


(b)

**PMG 13.4** Stomach—pylorus: (a) X5 and (b) X10 (H&E stain).



Comparison Between Fundus and Pylorus of the Stomach (Fig. 13.11; Table 13.1)



**Figure 13.11** Comparison between gastric glands of the fundus and pyloric regions (three-dimensional view). Note the difference between the depth of the gastric pit and the length of the glands; also note the difference between the coiling of the bases of the gastric glands of the two regions.

**Table 13.1** Comparison Between Fundus and Pylorus of the Stomach

Features	Fundus and body	Pylorus
Depth of the gastric pit	Less	More
Coiling of base of the gland	Less	More
Parietal cells	Numerous	Very few
Zymogen cells	Numerous	Absent

**SMALL INTESTINE**

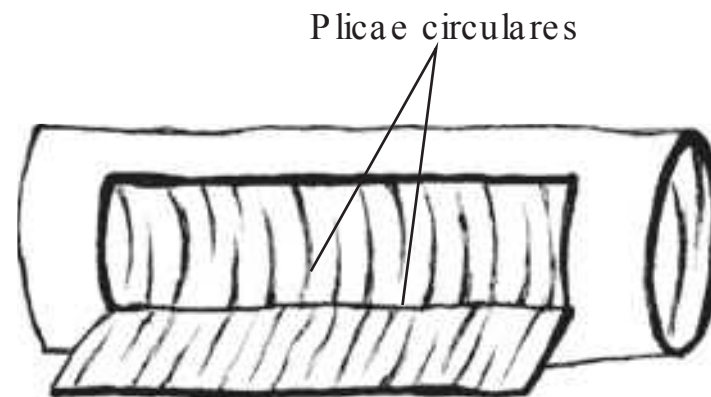
- The small intestine begins as a continuation of the pyloric end of the stomach and ends in the caecum (ileocaecal junction).
- It consists of three parts: duodenum, jejunum and ileum.
- The function of the small intestine is digestion and absorption of the digested food. It secretes several enzymes which help in digestion.

**MICROSCOPIC FEATURES**

- As mentioned previously, it is the mucosa in which changes are seen; other layers remain almost the same.
  - (a) Mucosa: This has been discussed subsequently.
  - (b) Submucosa
  - (c) Muscularis externa: These two layers remain almost the same as described under the section ‘General Microscopic Features of GIT’.
  - (d) The fourth layer: This is serosa except in the duodenum which is retroperitoneal; hence, the duodenum has both serosa and adventitia.

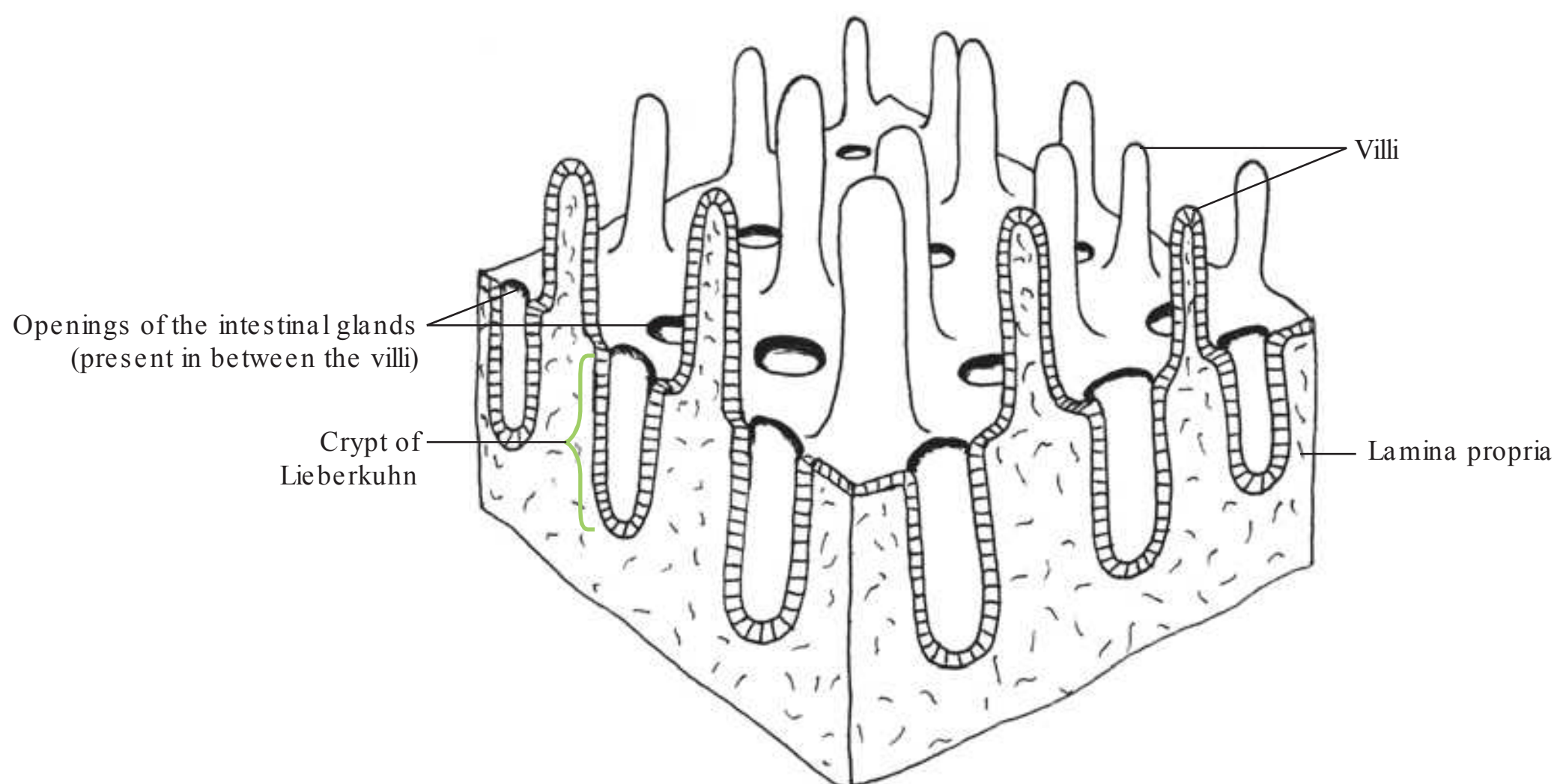
### Mucosa of the Small Intestine

- The luminal surface of the small intestine has numerous permanent folds projecting into the lumen called plicae circulares (singular: plica circulares) or valves of Kerckring (Fig. 13.12). These folds consist of mucosa and submucosa (PMG 13.5). They are visible macroscopically.



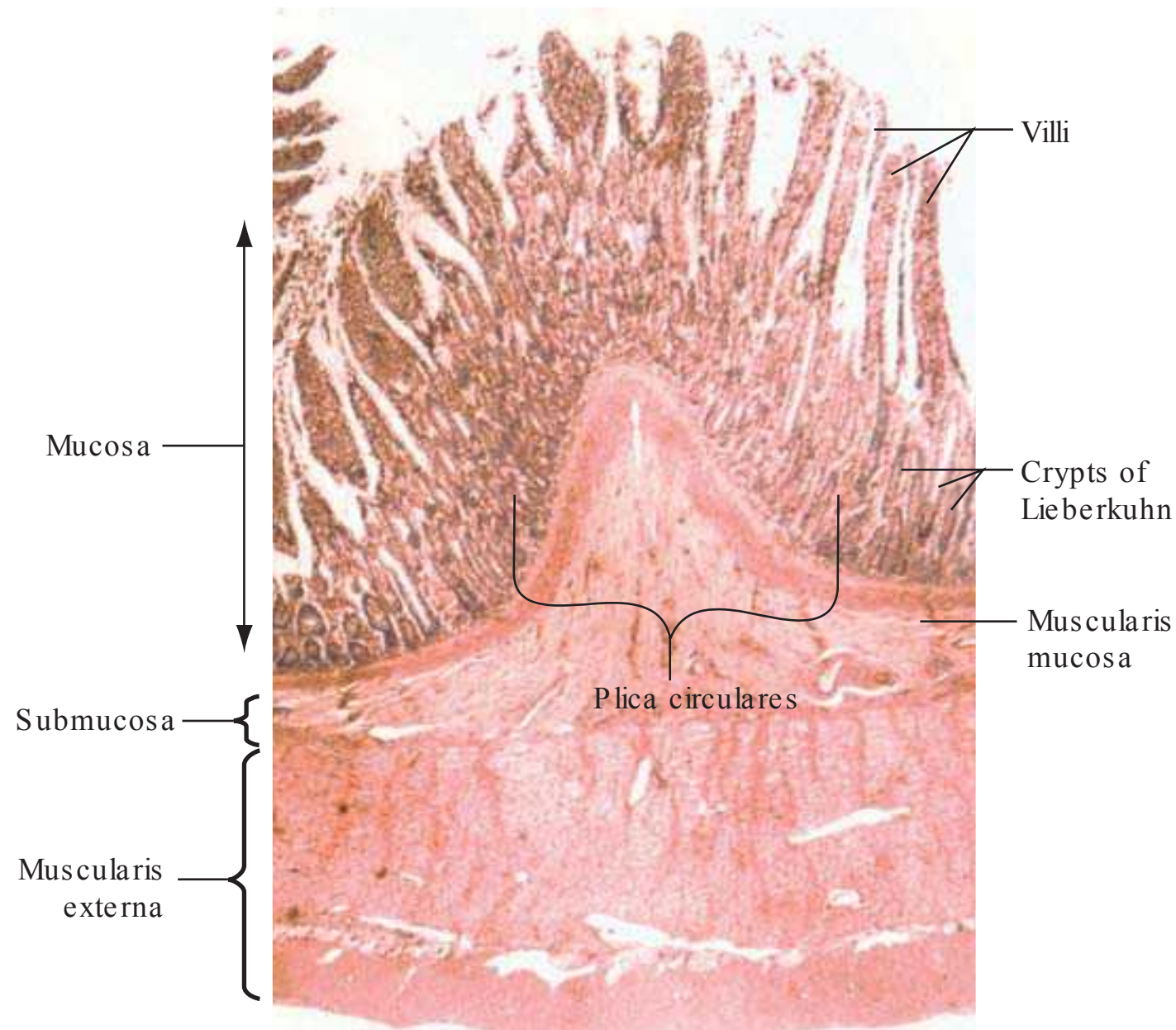
**Figure 13.12** Small intestine. The wall is cut open to show its luminal surface. Also seen are plicae circulares—these are permanent folds projecting into the lumen; they consist of mucosa and submucosa.

- The mucosa shows numerous finger-like projections into the lumen called intestinal villi. These are projections of mucosa and each villus consists of a core of lamina propria covered with epithelium.
- It should be noted that a villus does not have a core of submucosa whereas plica circulares has both mucosa and submucosa.
- In between the villi, there are openings of intestinal glands; these glands are also called crypts of Lieberkuhn. These are simple tubular glands present in the lamina propria (Fig. 13.13; PMG 13.5).



**Figure 13.13** Three-dimensional view of small intestine. Villi and opening of intestinal glands can be seen on the surface. On the cut surface, intestinal glands in the lamina propria are seen.

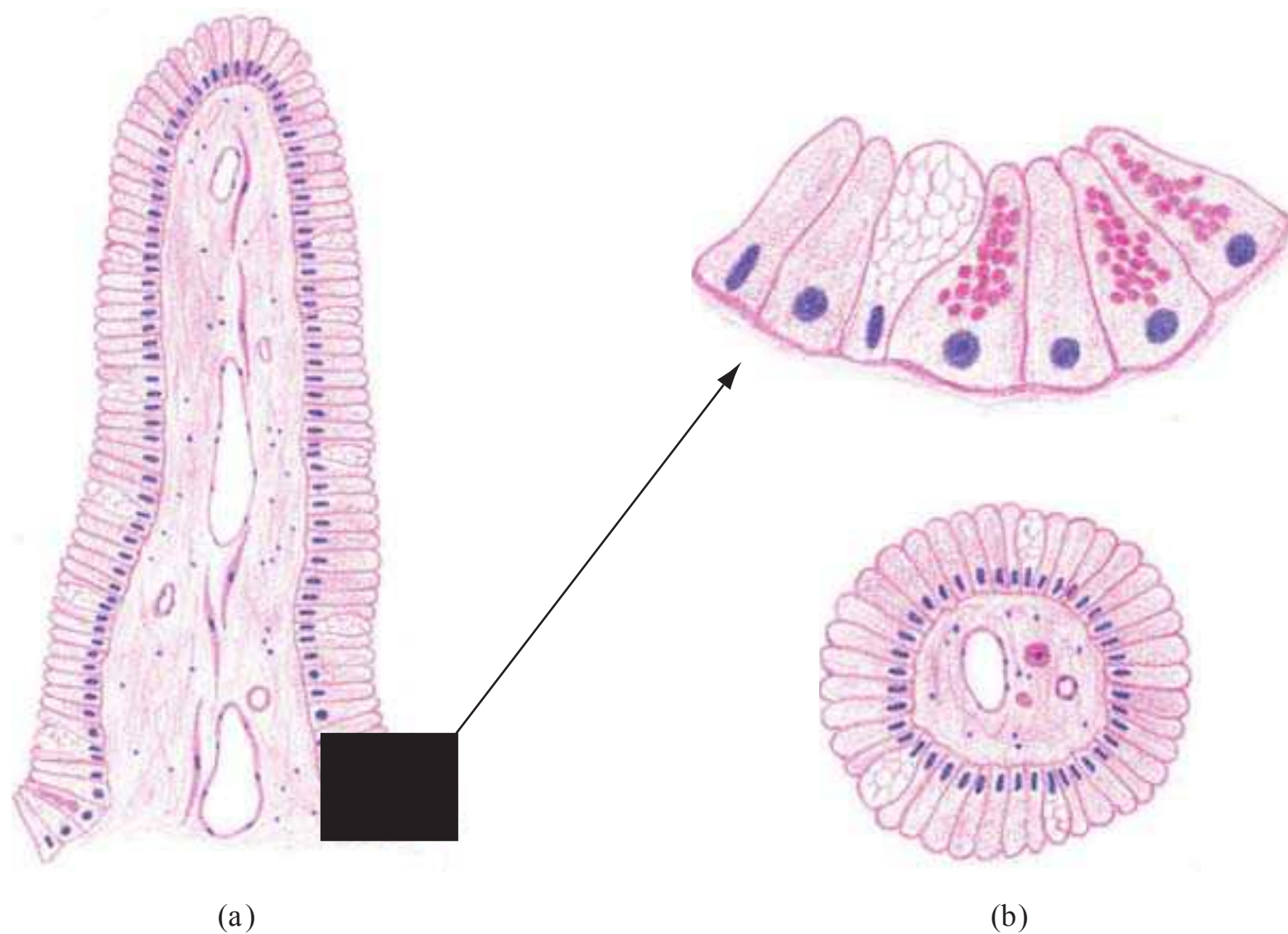




**PMG 13.5** Section of small intestine showing villi and plica (H&E stain, X2.5).

### *Intestinal Villi* (Figs 13.14 and 13.15)

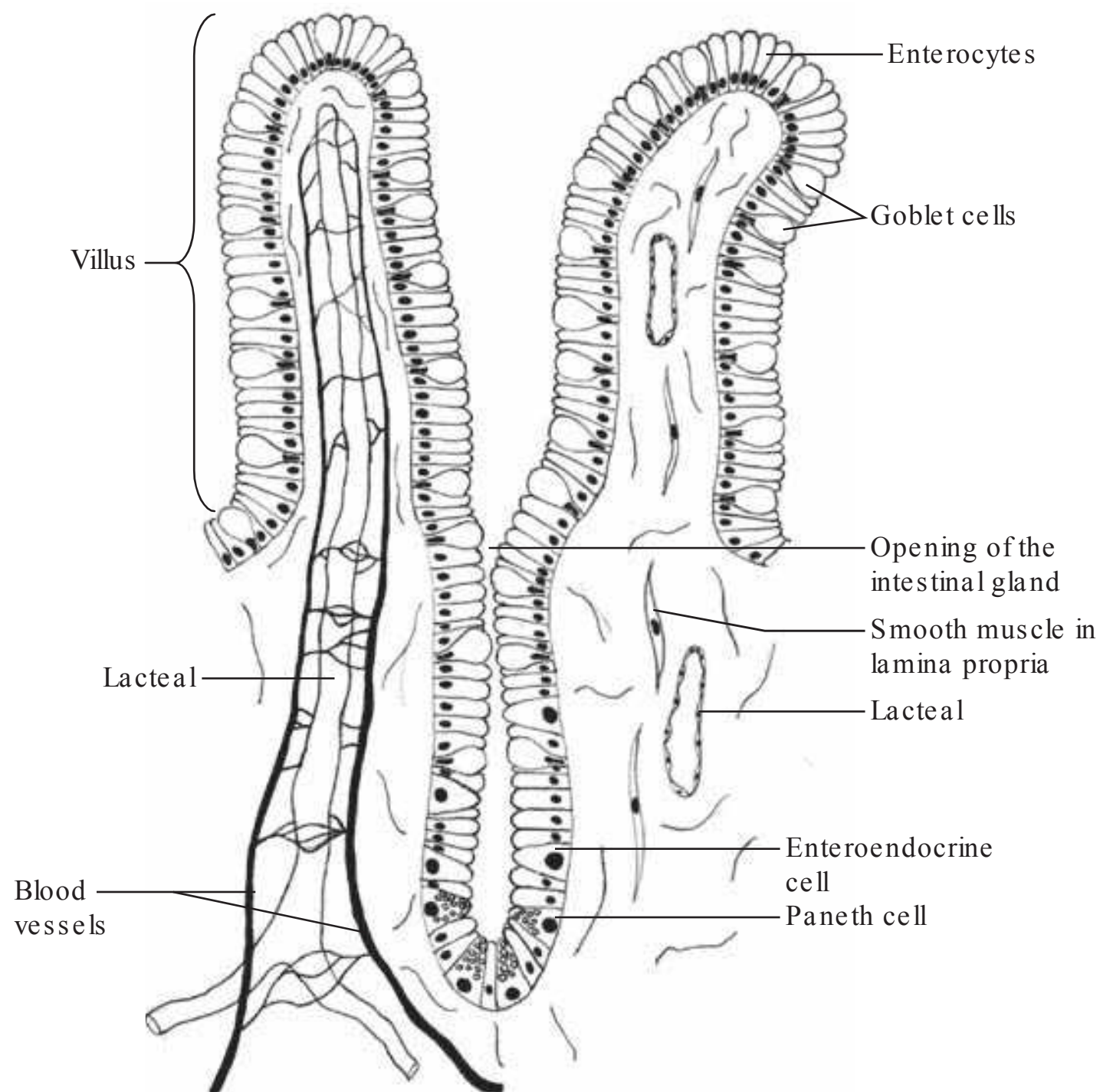
- Lining epithelium is simple columnar and composed of two types of cells, enterocytes and goblet cells (epithelium of stomach does not have goblet cells). Enterocytes are the absorptive cells.
- Goblet cells are scattered in between the enterocytes, and number of goblet cells increases distally in the intestinal tract.
- The luminal surface of the enterocytes has microvilli. These microvilli give striated appearance to the luminal surface which is called striated border or brush border.



**Figure 13.14** Section of villus and crypt of Lieberkuhn. (a) Longitudinal section—inset shows the paneth and enteroendocrine cells of crypt of Lieberkuhn. (b) Transverse section of villus. (H&E pencil drawing)



- All these changes in the mucosa—plicae circulares, intestinal villi and microvilli—increase the surface area for absorption of digested food.
- Within the villi, in the centre of the core of the lamina propria, there is a large lymphatic vessel called lacteal. The function of lacteal is absorption of lipids.
- Some smooth muscles also extend from muscularis mucosa into the villus core; they run along the central axis of the villus. These smooth muscles in the villus allow it to contract intermittently.



**Figure 13.15** Schematic diagram of villi and crypt of Lieberkuhn.

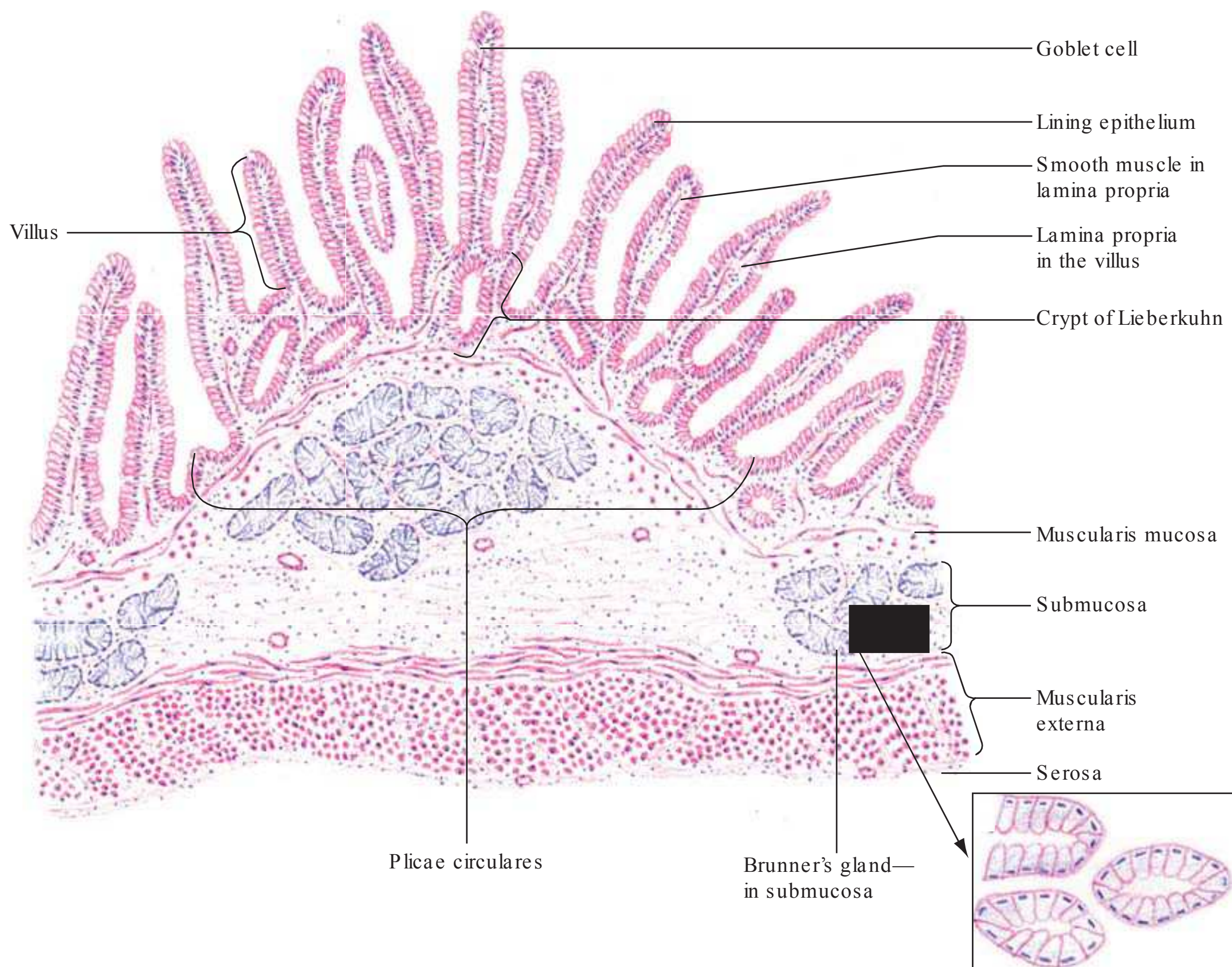
#### *Intestinal Glands/Crypts of Lieberkuhn* (Figs 13.14 and 13.15)

- Intestinal glands consist of mainly enterocytes and goblet cells. Apart from these cells, they have Paneth cells, enteroendocrine cells and stem cells.
- Paneth cells are present at the base of the intestinal glands. They are pyramidal in shape with basal nuclei, and their cytoplasm contains numerous eosinophilic granules. These cells secrete lysozyme and a substance called defensins which provides some protection against infection.
- Enteroendocrine cells are present at the base of intestinal glands and they produce hormones.
- Stem cells are located in the lower half of the intestinal glands. The new epithelial cells are formed from the stem cells, and they migrate upwards and reach the tips of the villi. These cells have rapid turnover and are shed after about every 5 days.



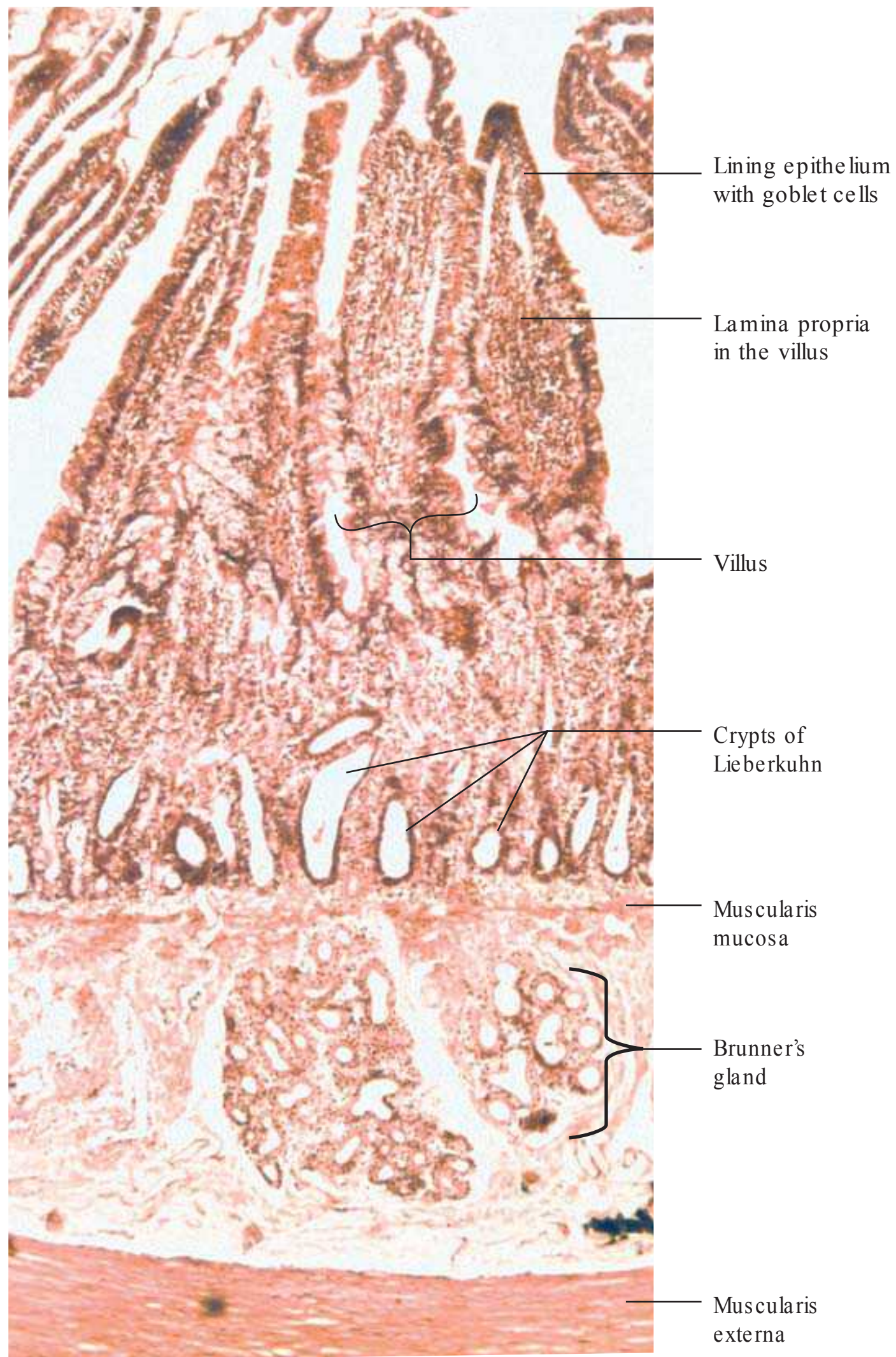
**DUODENUM** (Fig. 13.16; PMG 13.6)

- Histology of the duodenum has been described above in the general discussion on small intestine. The special features of duodenum are as follows:
  - (a) Leaf-shaped villi
  - (b) Submucosa has duodenal glands or Brunner's glands. Cells of Brunner's glands are columnar with a flat nucleus at the base. The ducts of these glands open into the crypts of Lieberkuhn after passing through muscularis mucosa and lamina propria. They secrete alkaline mucus, which protects the duodenal mucosa from the acidic chyme and provides alkaline medium for the pancreatic enzymes to be active.



**Figure 13.16** Section of duodenum in low magnification. Inset shows the Brunner's glands; note the columnar cells with flat nucleus at their bases. (H&E pencil drawing)



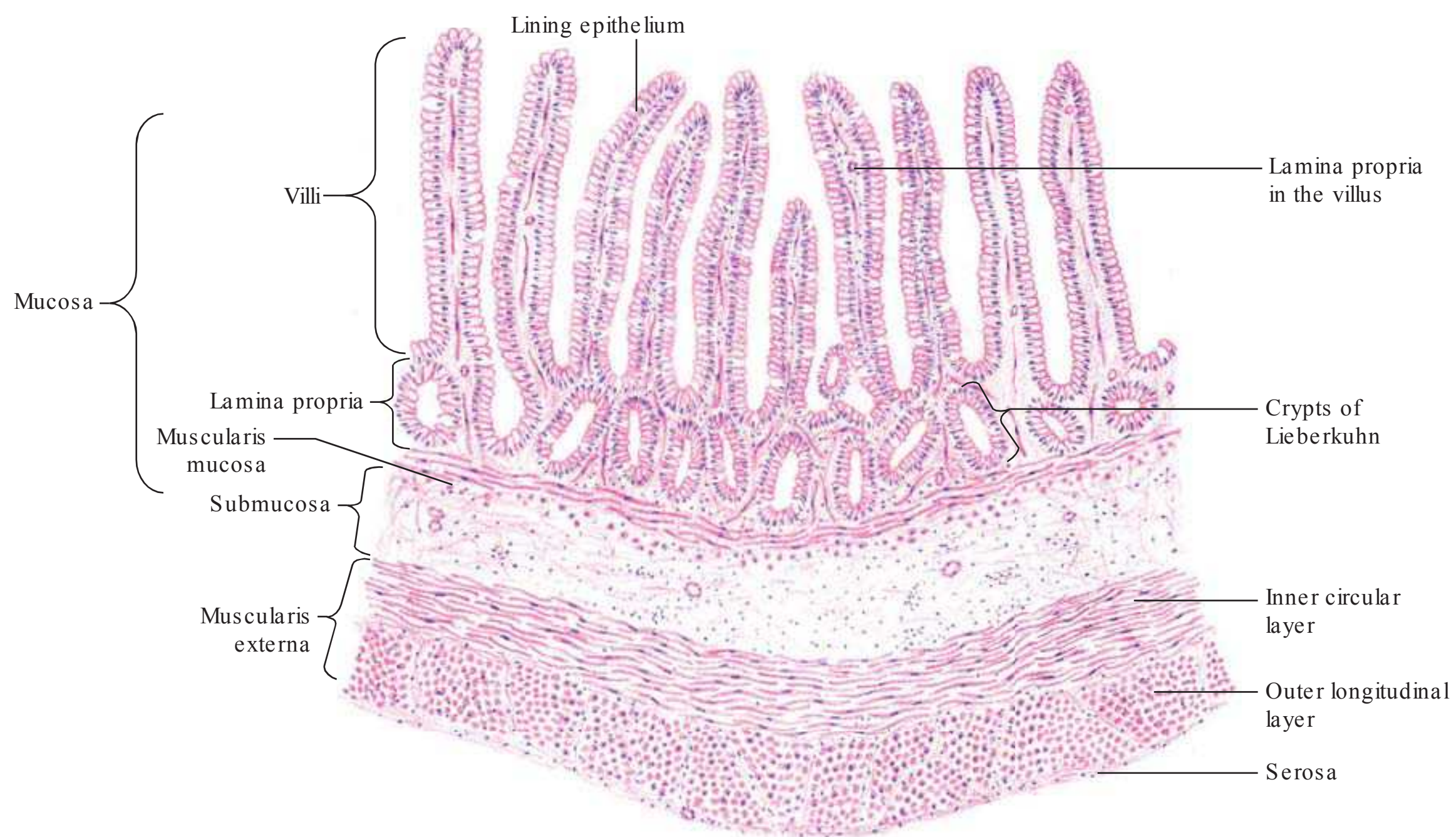


**PMG 13.6** Section of the duodenum (H&E stain, X5).

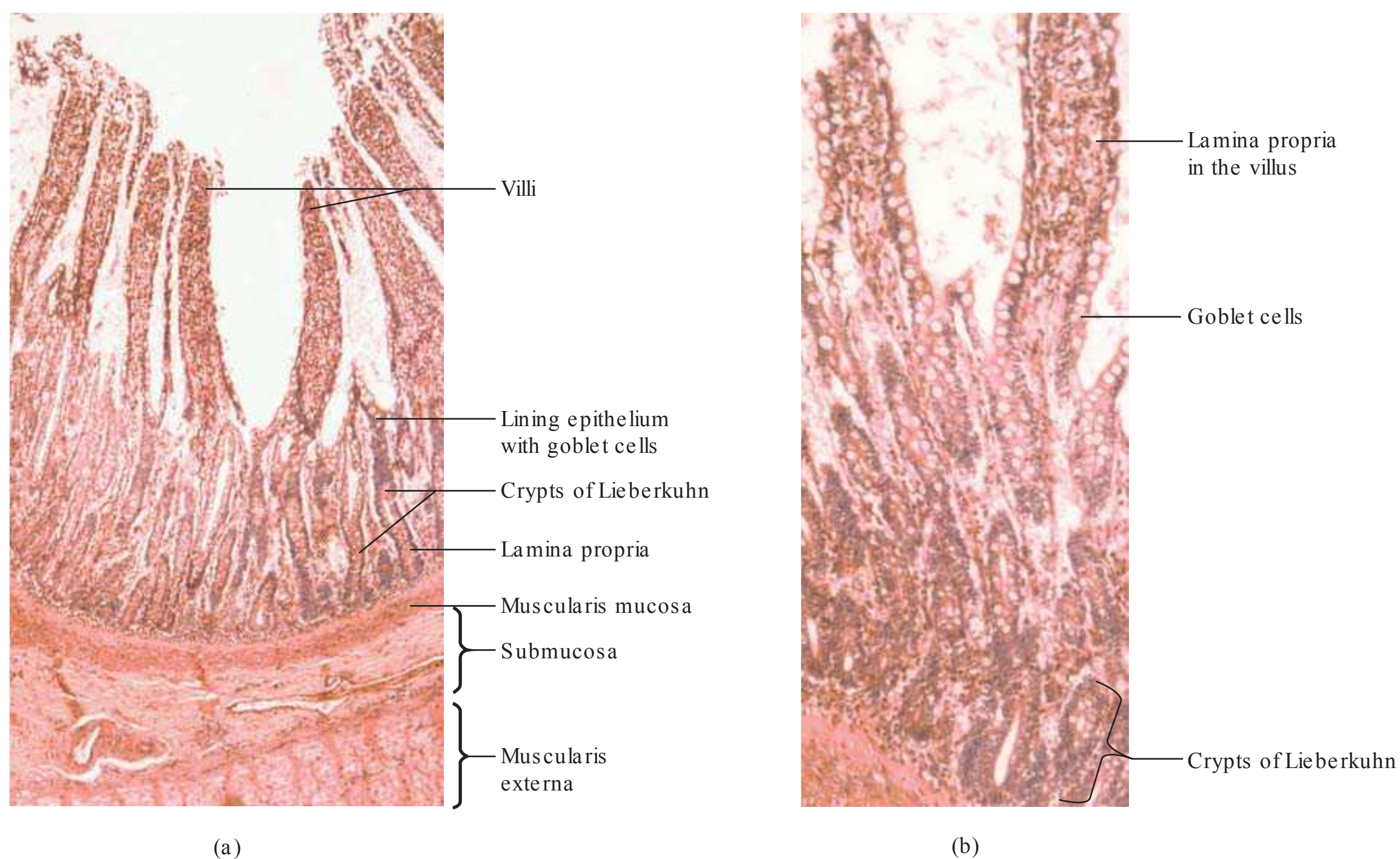
**JEJUNUM** (Fig. 13.17; PMG 13.5 and 13.7)

- Special features are as follows:
  - (a) Tongue-shaped villi





**Figure 13.17** Section of the jejunum in low magnification (H&E pencil drawing).

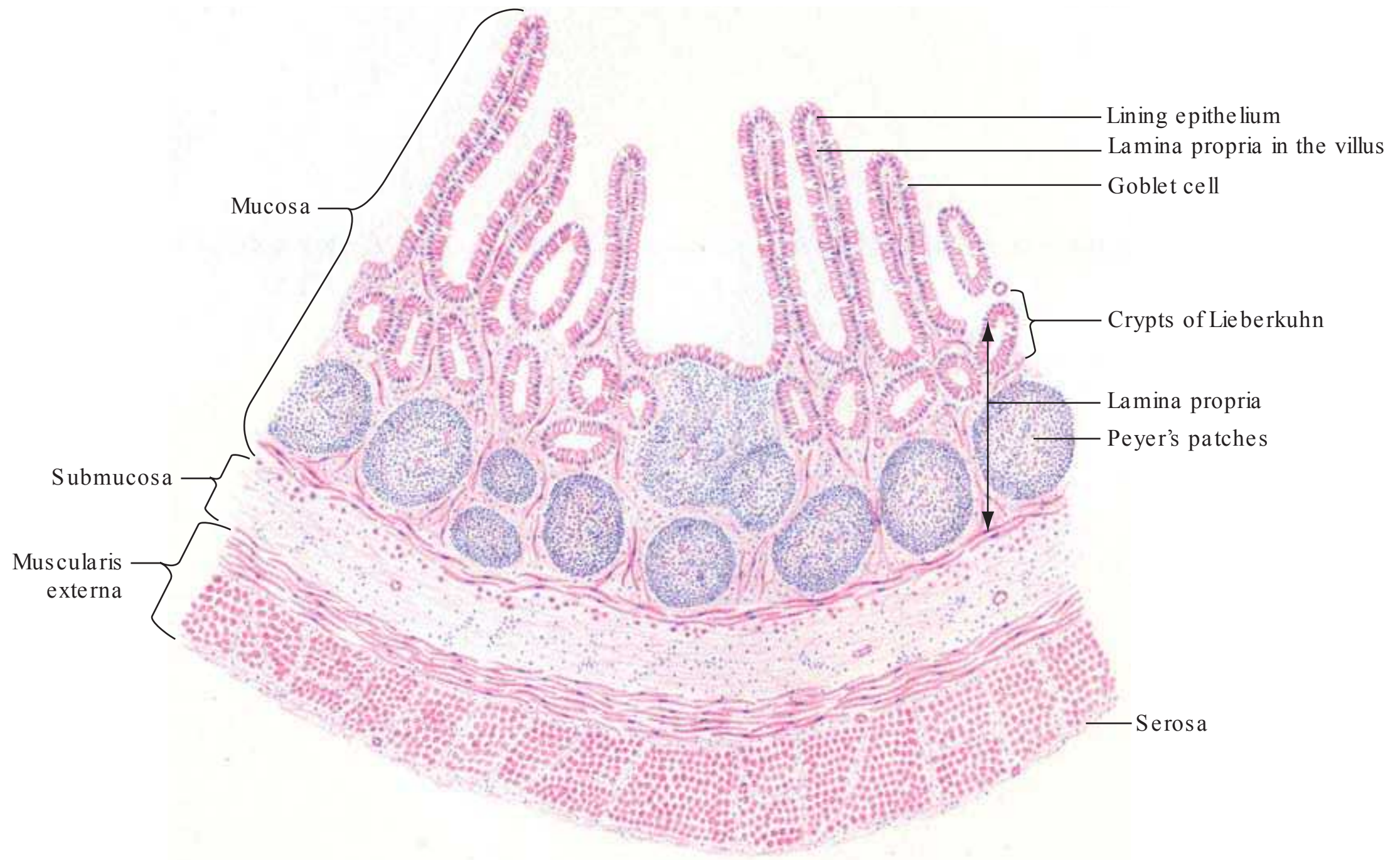


**PMG 13.7** Section of the jejunum: (a) X5 and (b) X10 (H&E stain).

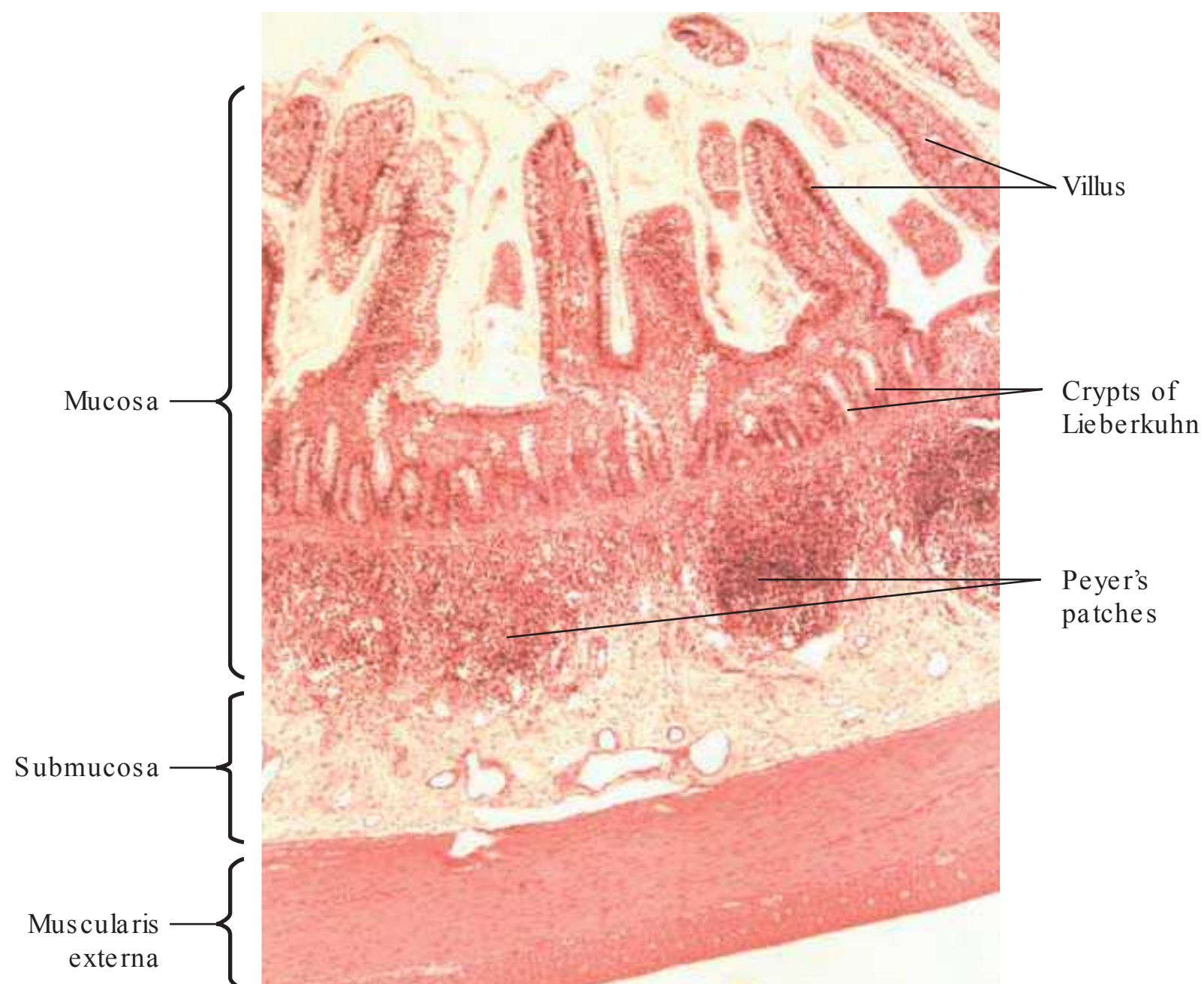


**ILEUM** (Fig. 13.18; PMG 13.8)

- The special features are as follows:
  - Finger-shaped villi, short and less in number.
  - Lamina propria shows numerous lymphoid follicles called Peyer's patches.



**Figure 13.18** Section of the ileum in low magnification (H&E pencil drawing).



**PMG 13.8** Section of the ileum (H&E stain, X5).

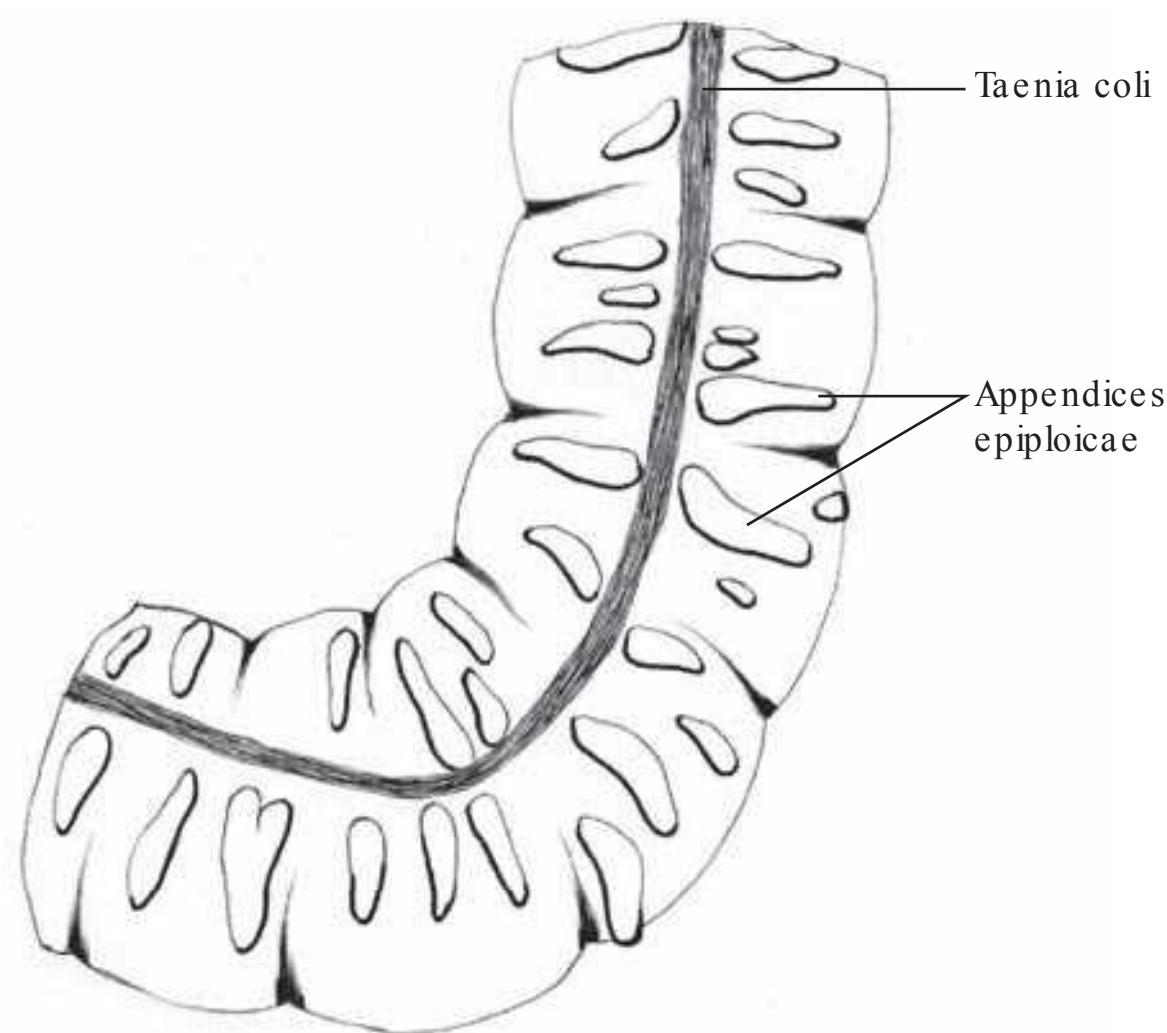


## COMPARISON OF PARTS OF SMALL INTESTINE

- Duodenum: It has Brunner's gland in submucosa.
- Ileum: It has numerous lymphoid follicles in lamina propria.
- Jejunum: It is the part of small intestine without Brunner's gland or lymphoid follicles.

## LARGE INTESTINE

- The large intestine consists of caecum, colon, rectum and anal canal.
- The main functions of the large intestine are absorption of water and conversion of the liquid, undigested material into solid faeces.
- The diameter of the large intestine is more than that of the small intestine.
- Except the anal canal, the structure of the large intestine remains almost the same throughout.
- In most of the large intestine, the peritoneum shows outpouchings containing fat; these are called appendices epiploicae (Fig. 13.19).



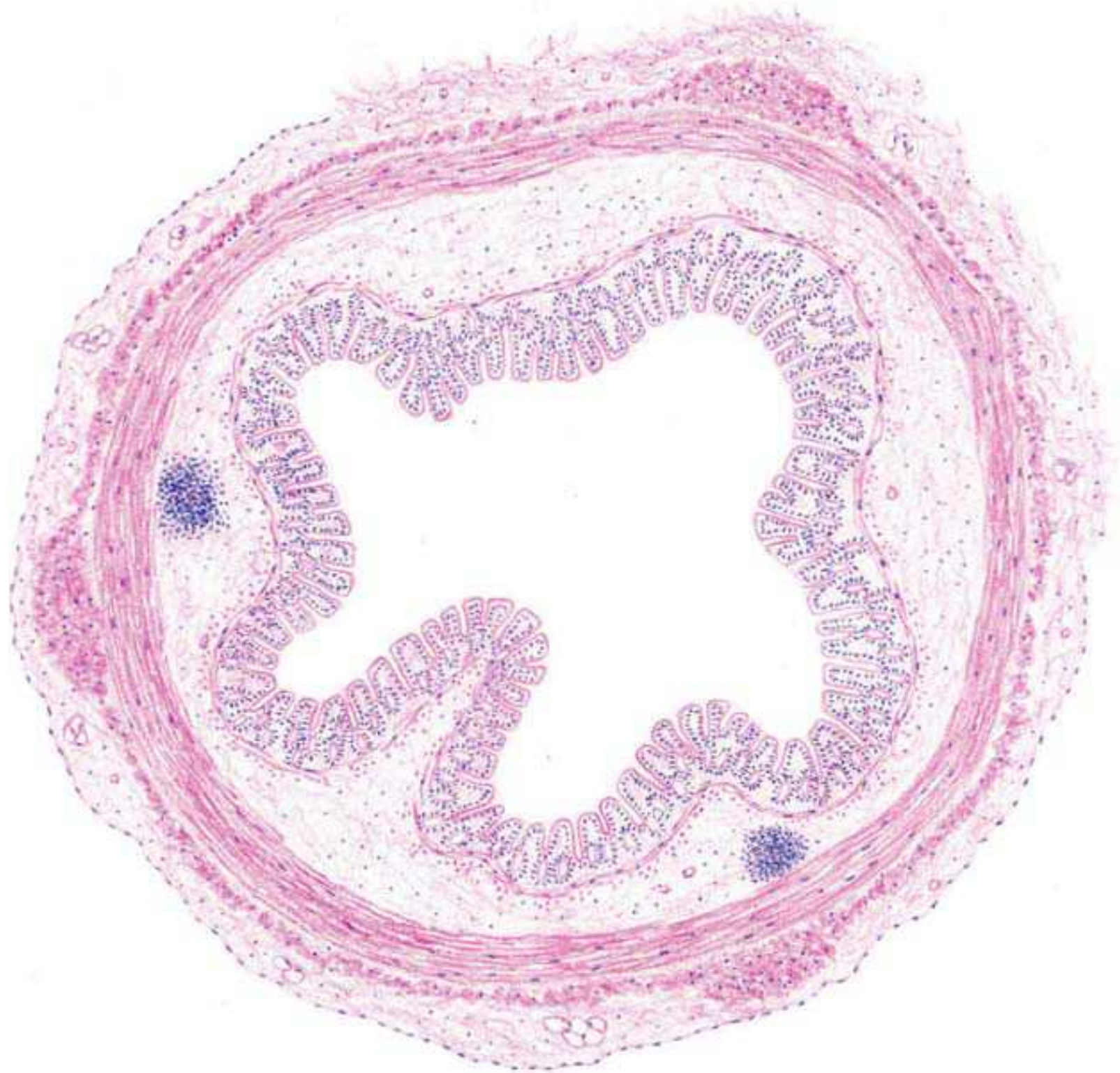
**Figure 13.19** Large intestine.

## COLON

The microscopic features are described in the following text.

### **Mucosa** (Figs 13.20 and 13.21; PMG 13.9 and 13.10)

- Mucosa is folded in non-distended state.
- It has no villi and plicaeulares.
- The epithelium is simple columnar with more goblet cells than in the small intestine.
- Absorptive cells have microvilli.
- Crypts of Lieberkuhn have more goblet cells than the crypts of the small intestine. The glands also contain enteroendocrine cells and stem cells, which are both located in the lower part of the glands. However, there are no Paneth cells.
- Lamina propria has numerous lymphoid follicles.



**Figure 13.20** Panoramic view of large intestine (H&E pencil drawing).

### **Submucosa**

- It is the same as described under the section ‘General Microscopic Features of GIT’

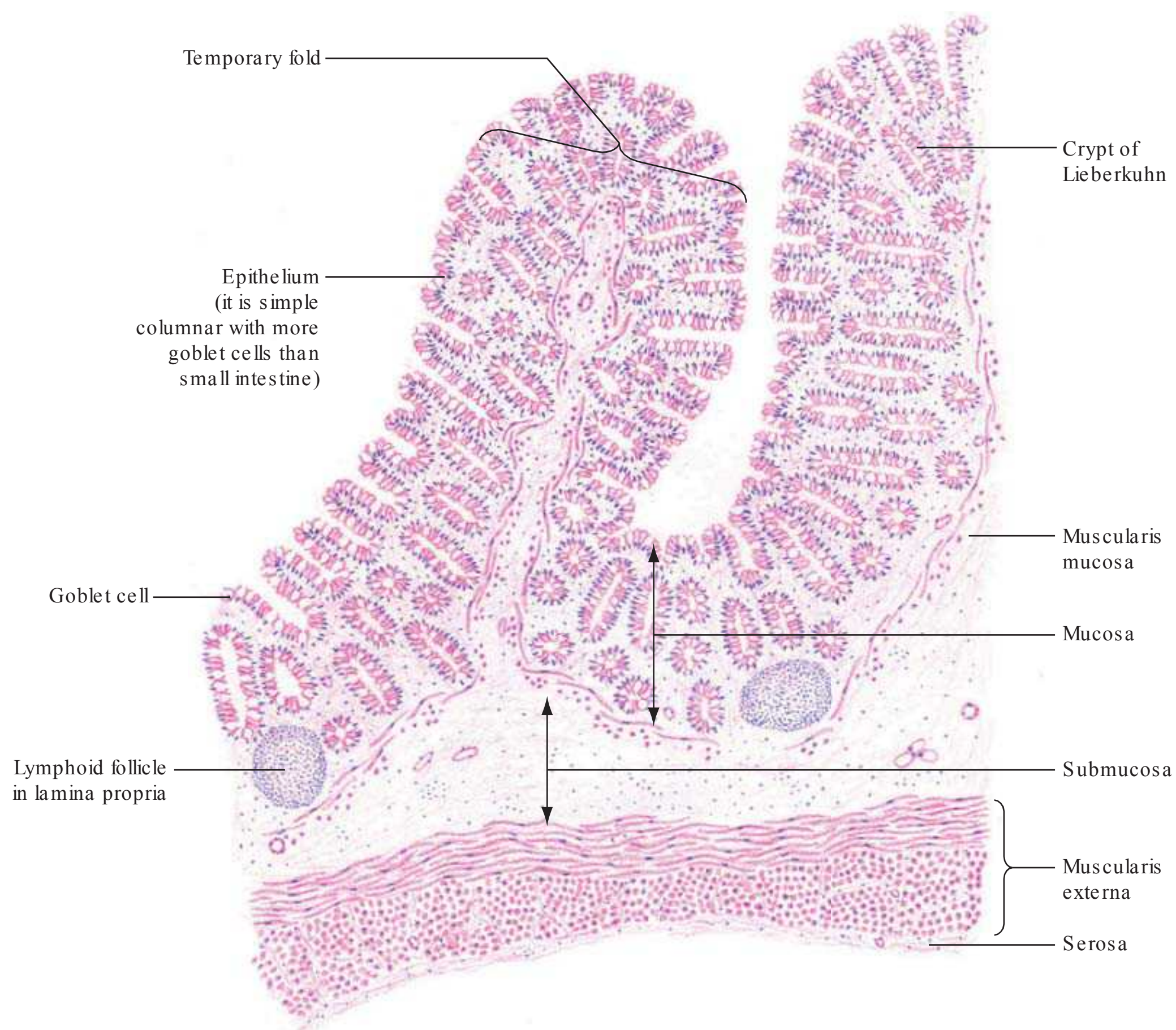
### **Muscularis Externa**

- It consists of inner circular and outer longitudinal layers; in addition to this, the outer longitudinal layer forms three longitudinal bands called taenia coli (Figs 13.19 and 13.20).

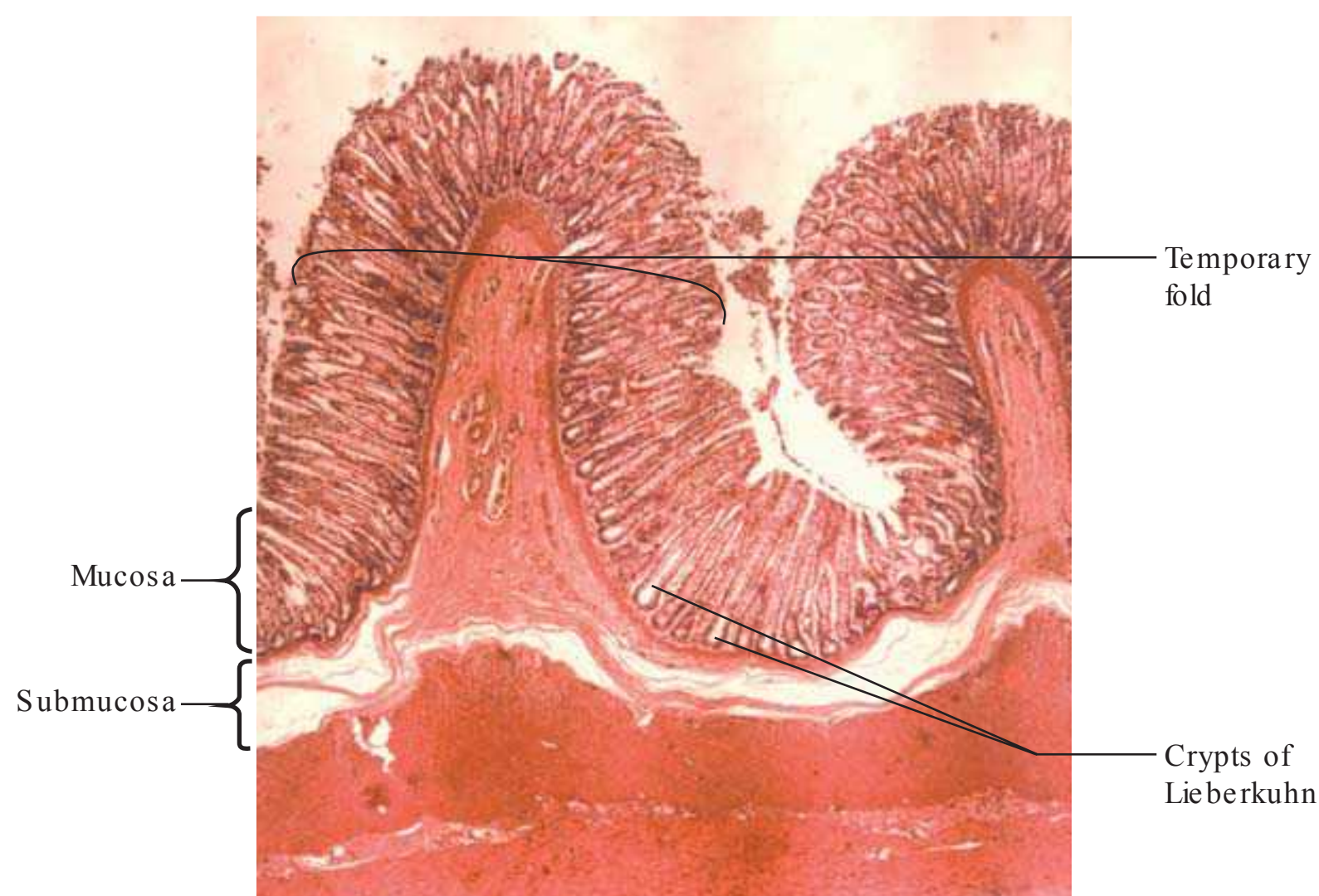
### **Fourth Layer (Adventitia or Serosa)**

- Intraperitoneal parts (transverse and sigmoid colon) have serosa, and retroperitoneal parts (ascending and descending colon) have both serosa and adventitia.



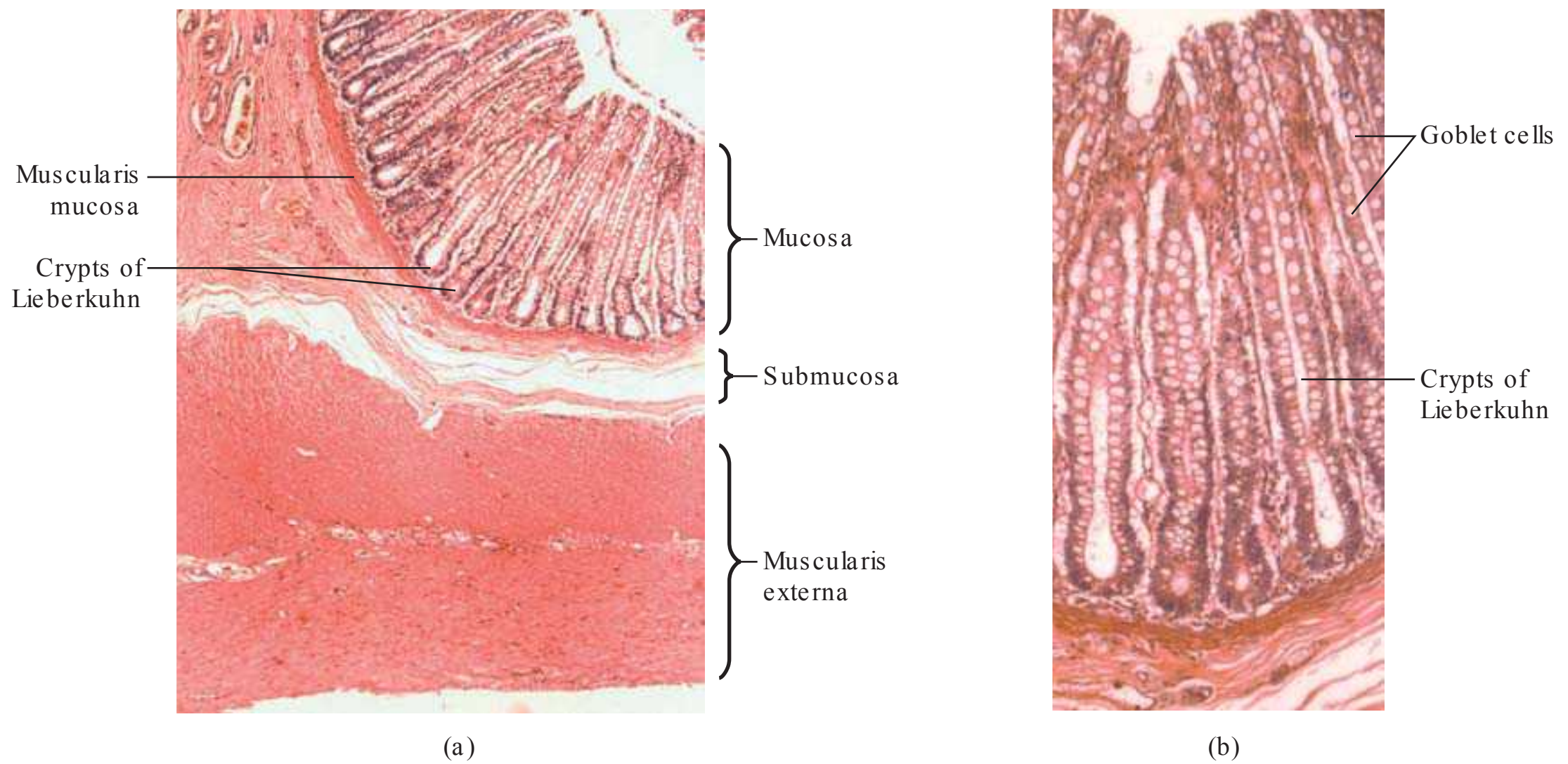


**Figure 13.21** Section of the large intestine in low magnification (H&E pencil drawing).



**PMG 13.9** Section of the colon (H&E stain, X2.5).

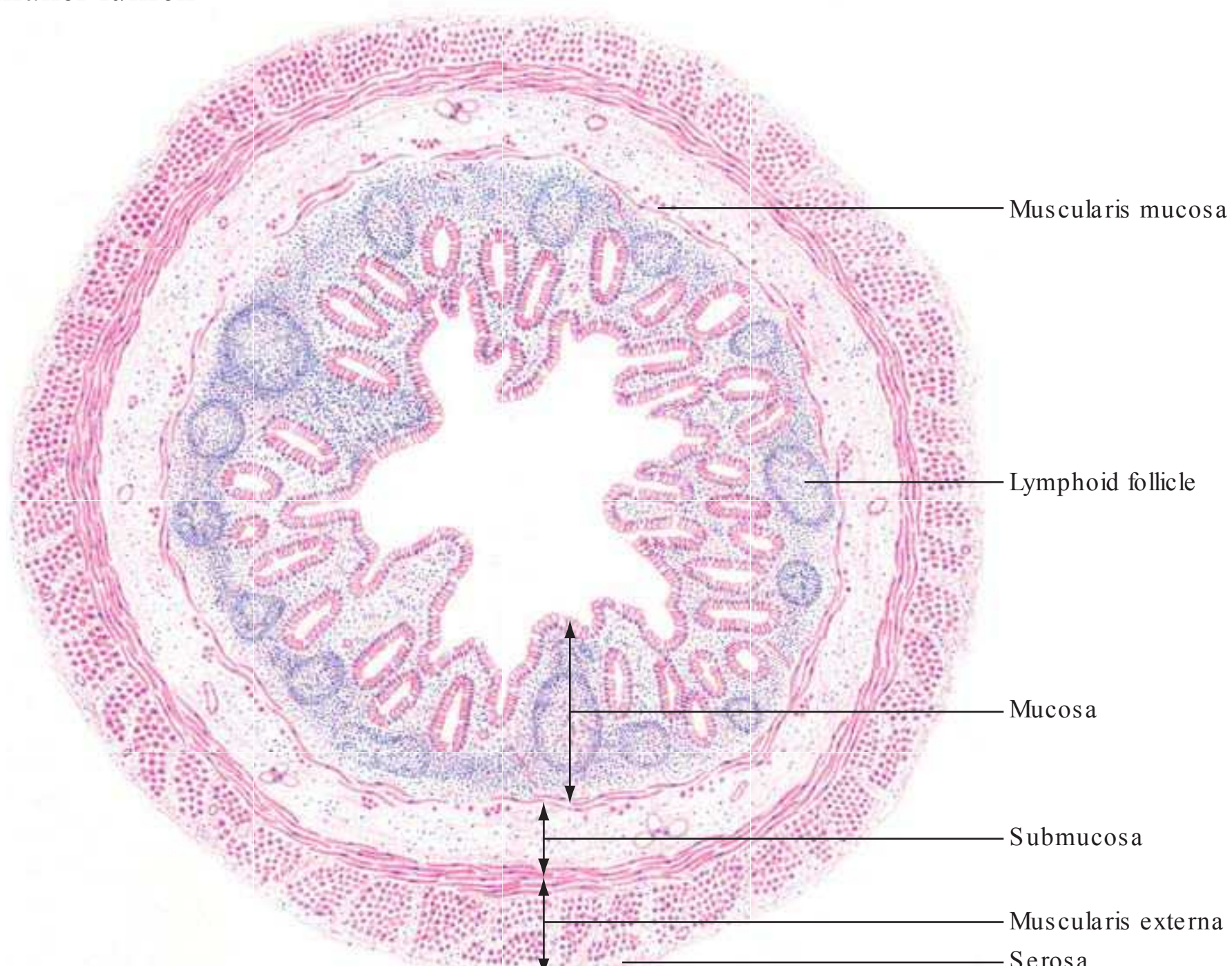




**PMG 13.10** Section of the colon: (a) X5 and (b) X10 (H&E stain).

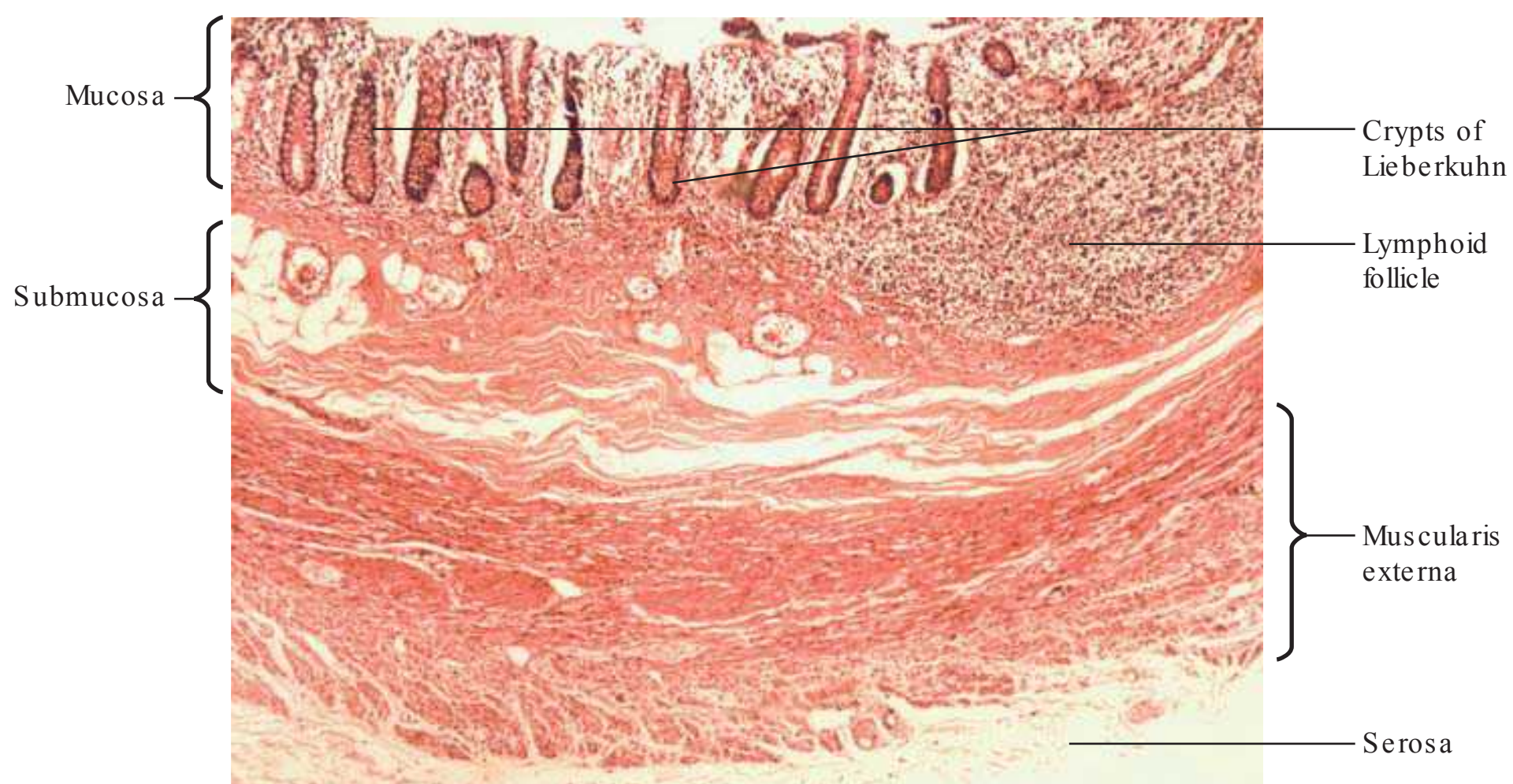
#### **APPENDIX** (Fig. 13.22; PMG 13.11)

- The microscopic structure of appendix resembles the colon with a few differences which are listed as follows:
  - Lamina propria has numerous lymphoid follicles which extend into submucosa
  - No taenia coli (Fig. 13.22)
  - Smaller lumen



**Figure 13.22** Section of the appendix in low magnification (H&E pencil drawing).

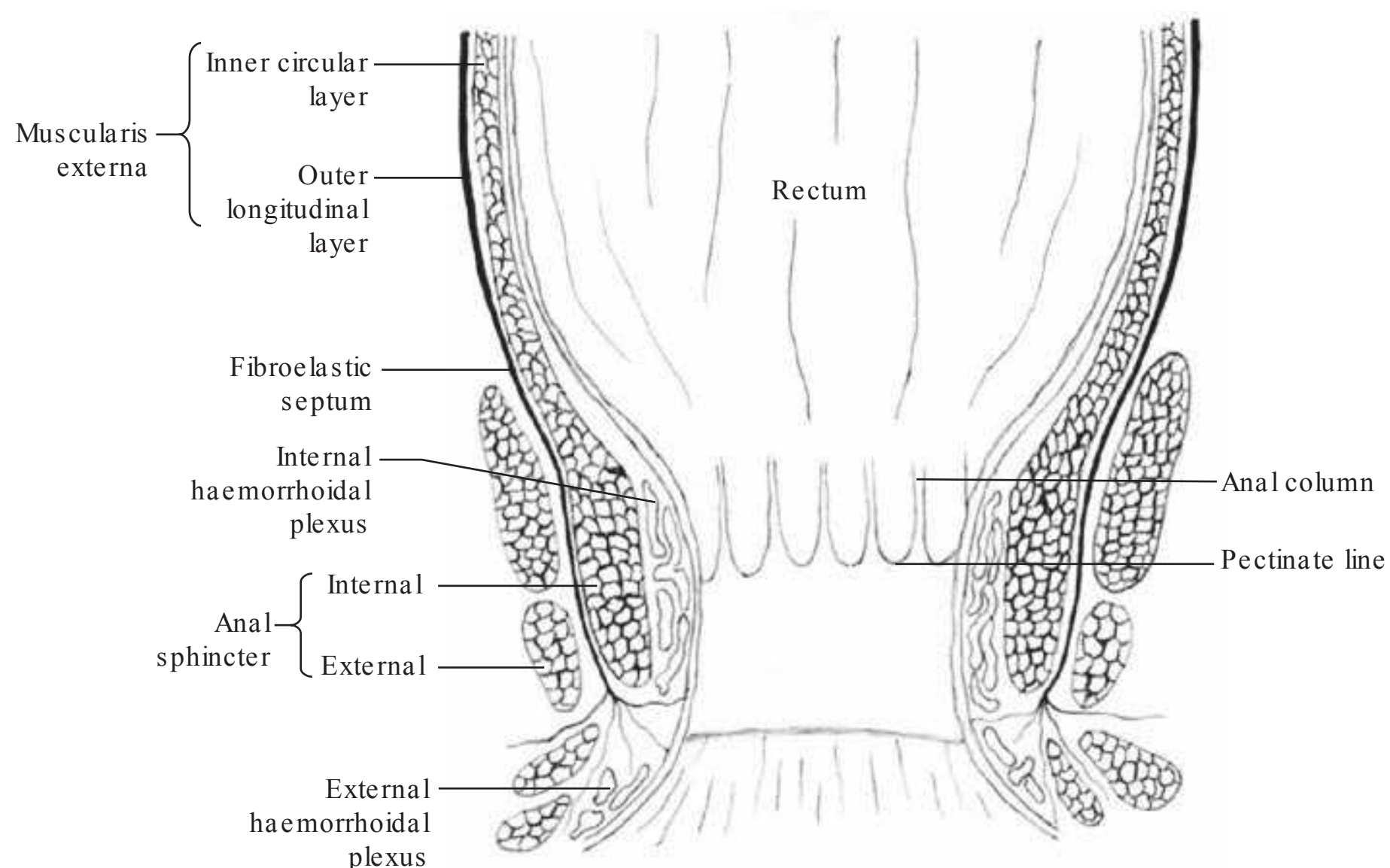




**PMG 13.11** Section of the appendix (H&E stain, X5).

### ANAL CANAL (Fig. 13.23)

- In the upper part of anal canal, the mucosa shows 6–10 permanent longitudinal folds known as anal columns of Morgagni.
- Lower ends of columns of Morgagni are connected by folds of mucosa; these are anal valves.
- The pectinate line corresponds to the level of the anal valves.



**Figure 13.23** Anal canal.

## Microscopic Features

### 1. Mucosa

- The lining epithelium changes from simple columnar (as in colon) to stratified squamous non-keratinised at the pectinate line.
- In the lower part of the anal canal, the epithelium changes from stratified squamous non-keratinised to stratified squamous keratinised epithelium (epidermis). In this region of the anal canal, underneath the epithelium, there are numerous apocrine sweat glands, the circumanal glands.

### 2. Submucosa

- The submucosa has numerous venous plexuses, the haemorrhoidal plexuses (Fig. 13.23).

### 3. Muscularis externa

- The inner circular layer of muscularis externa forms the internal anal sphincter (involuntary) and the longitudinal layer forms thin sheets which get attached to the perianal skin.
- The external anal sphincter consists of skeletal muscle; it is under voluntary control.

### 4. Fourth layer

- Fourth layer is adventitia.

## CLINICAL CORRELATES

### Barrett's Oesophagus

- Barrett's oesophagus is a complication of longstanding gastro-oesophageal reflux (reflux of gastric contents into the oesophagus) due to chronic irritation of mucosa. The squamous epithelium at the lower end of oesophagus is replaced by the columnar epithelium. This condition is known as Barrett's oesophagus and it is one of the risk factors for oesophageal cancer.

### Gastric Ulcer

- Breach in the mucosa of stomach is called gastric ulcer. There are several factors responsible for gastric ulcer (cigarettes, alcohol, aspirin, etc.). The most important factor is infection with bacteria called *Helicobacter pylori*. The gastric ulcer can be benign or malignant.

### Duodenal Ulcer

- Like in the stomach, ulcers can occur in the duodenum also. Unlike gastric ulcers which may turn malignant, duodenal ulcers never become malignant.

### Celiac Disease

- Celiac disease is also called gluten-sensitive enteropathy. It results from sensitivity to gluten protein which is present in wheat. Damage to intestinal villi results in malabsorption. The patient is advised to take gluten-free diet.

### Typhoid Ulcer

- Typhoid is caused by bacteria called *Salmonella*. It invades the epithelium of ileum and causes ulceration and swelling in lymphoid tissues.

### Ulcerative Colitis

- Ulcerative colitis is one of the inflammatory bowel diseases more common in females. Inflammation and ulceration occurs in the colon and rectum. Damage to mucosa and submucosa results in bloody diarrhoea.

### Hirschsprung Disease

- The neural plexus of the GIT (Meissner's and myenteric plexus) develops from neural crest cells which migrate into the wall of the GIT in cephalocaudal direction during development. This disease results when migration of neural cells arrests before reaching the anus. There is no neural coordination in the aganglionic segment; hence, it remains contracted, and this leads to constipation and abdominal distension.

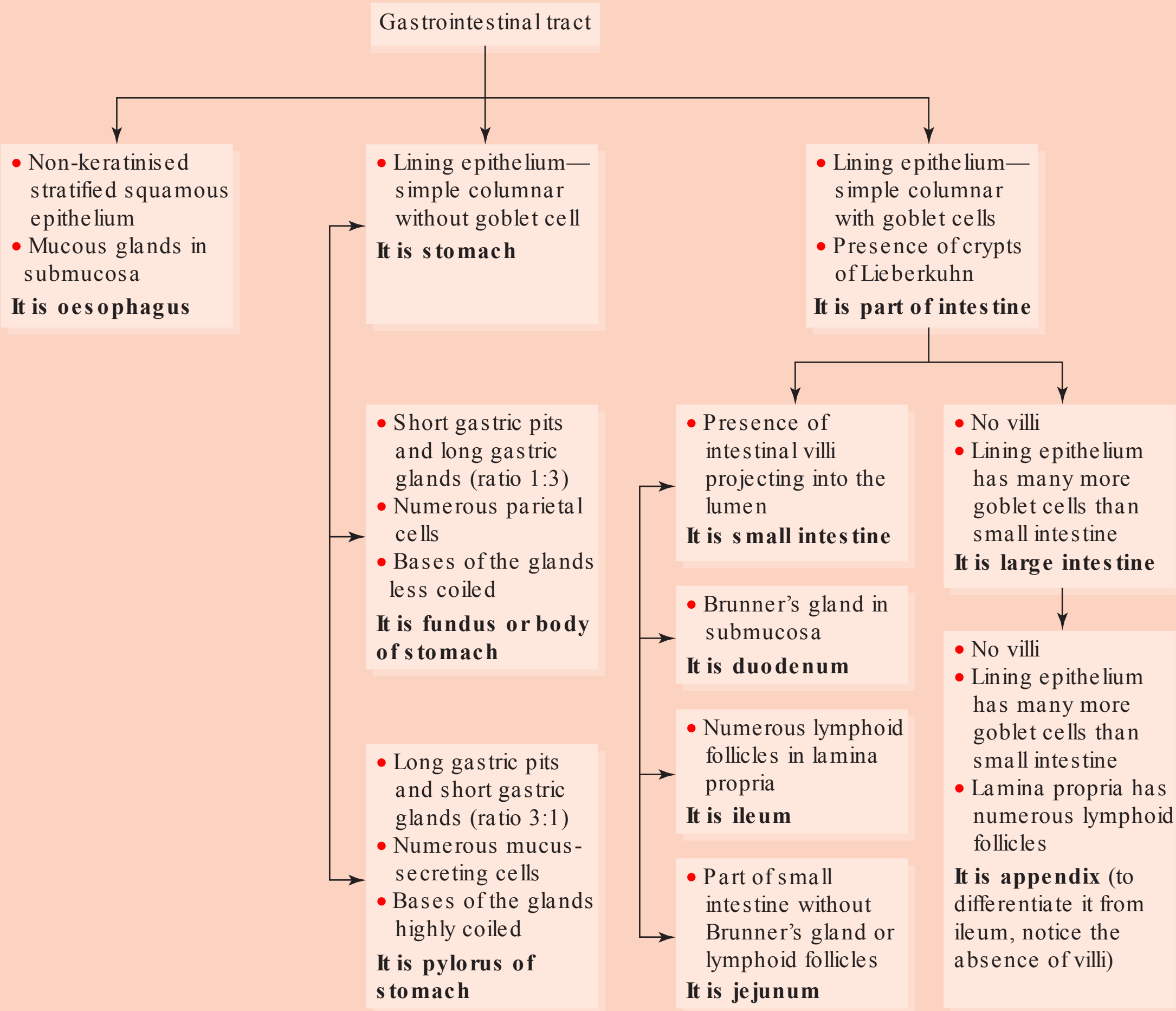
### Appendicitis

- Inflammation of the appendix is called appendicitis. In this condition numerous neutrophils and ulcerations are seen in mucosa.



KEYPOINTS

Key Points for Histology Slide Identification



Microscopic Features of Different Parts of GIT

Part of GIT	Epithelium	Lamina propria	Special features in other layers
Oesophagus (Fig. 13.4; PMG 13.1)	• Non-keratinised stratified squamous	• A few lymphoid follicles	• Submucosa has mucous glands • Muscularis externa in upper one-third skeletal muscle, in middle one-third both skeletal and smooth muscles and in lower one-third smooth muscle
Stomach—fundus and body (Figs 13.6 and 13.7; PMG 13.3)	• Simple columnar	• Short gastric pits • Gastric glands—less coiled at base, numerous parietal and zymogen cells	• Muscularis externa has three layers—inner oblique, middle circular and outer longitudinal layers
Stomach—pylorus (Figs 13.9 and 13.10; PMG 13.4)	• Simple columnar	• Long gastric pits • Gastric glands—more coiled at the base, very few parietal cells, no zymogen cells	

(continued)

(continued)

Part of GIT	Epithelium	Lamina propria	Special features in other layers
Duodenum (Fig. 13.16; PMG 13.6)	<ul style="list-style-type: none"> <li>• Simple columnar</li> <li>• Goblet cells</li> <li>• Microvilli</li> </ul>	<ul style="list-style-type: none"> <li>• Crypts of Lieberkuhn</li> <li>• Villi</li> </ul>	<ul style="list-style-type: none"> <li>• Plica circulares</li> <li>• Brunner's glands in submucosa</li> </ul>
Jejunum (Fig. 13.17; PMG 13.5 and 13.7)		<ul style="list-style-type: none"> <li>• Crypts of Lieberkuhn</li> <li>• Villi</li> </ul>	<ul style="list-style-type: none"> <li>• Plica circulares</li> </ul>
Ileum (Fig. 13.18; PMG 13.8)		<ul style="list-style-type: none"> <li>• Crypts of Lieberkuhn</li> <li>• Villi</li> <li>• Peyer's patches</li> </ul>	<ul style="list-style-type: none"> <li>• Plica circulares</li> </ul>
Colon (Fig. 13.21; PMG 13.9 and 13.10)	<ul style="list-style-type: none"> <li>• Simple columnar</li> <li>• Numerous goblet cells</li> <li>• Microvilli</li> </ul>	<ul style="list-style-type: none"> <li>• Crypts of Lieberkuhn</li> </ul>	<ul style="list-style-type: none"> <li>• Taenia coli</li> </ul>
Appendix (Fig. 13.22; PMG 13.11)	<ul style="list-style-type: none"> <li>• Simple columnar</li> <li>• Numerous goblet cells</li> <li>• Microvilli</li> </ul>	<ul style="list-style-type: none"> <li>• Crypts of Lieberkuhn</li> <li>• Numerous lymphoid follicles</li> </ul>	<ul style="list-style-type: none"> <li>• No taenia coli</li> </ul>

## SELF-ASSESSMENT

1. Describe the general microscopic features of GIT.
2. Describe the gastric glands under the following headings: parts, types of cells and comparison between the gastric glands of fundus and pylorus.
3. Describe the general microscopic features of small intestine.
4. Compare the microscopic features of duodenum, jejunum and ileum.
5. Compare the mucosa of oesophagus, stomach, small intestine and large intestine



# Accessory Glands of the Gastrointestinal Tract

In this chapter, those glands are discussed which are situated outside the gastrointestinal tract but open within the tract. During embryonic development, these glands develop from the gastrointestinal tract as outpouching from its wall and retain their connection with it.

## SALIVARY GLANDS

- Salivary glands are the glands that secrete saliva. These glands can be major or minor.
- There are three pairs of major salivary glands: parotid, submandibular and sublingual.
- Minor salivary glands are numerous, located all over the oral mucosa, beneath the epithelium. Some of the minor salivary glands are the following:
  - (a) von Ebner's in tongue
  - (b) Glossopalatine in palatoglossal and palatopharyngeal arches
  - (c) Buccal glands in cheeks
  - (d) Labial glands in lips
- Secretion of salivary glands is known as saliva; around 1 L of saliva is produced every day.
- Functions of saliva: These include lubricating the luminal surface of the upper aerodigestive tract, moistening the food to help in deglutination and initiating digestion of carbohydrates by the enzyme salivary amylase present in it. Saliva also acts as a bactericidal due to the presence of lysozyme and immunoglobulin A.

## GENERAL STRUCTURE OF MAJOR SALIVARY GLANDS

Basically, a salivary gland consists of stroma, parenchyma and a duct system which carries the secretions into the oral cavity.

### Stroma

- The stroma consists of connective tissue capsule and septa.
- Numerous septa arise from the capsule and enter the parenchyma of the gland, dividing the gland into numerous lobules.
- These septa bring the blood vessels and nerves into the gland. Large ducts of the glands are also present in it.

### Parenchyma

- Parenchyma has two components: the secretory part and myoepithelial cells.

*Secretory Part*

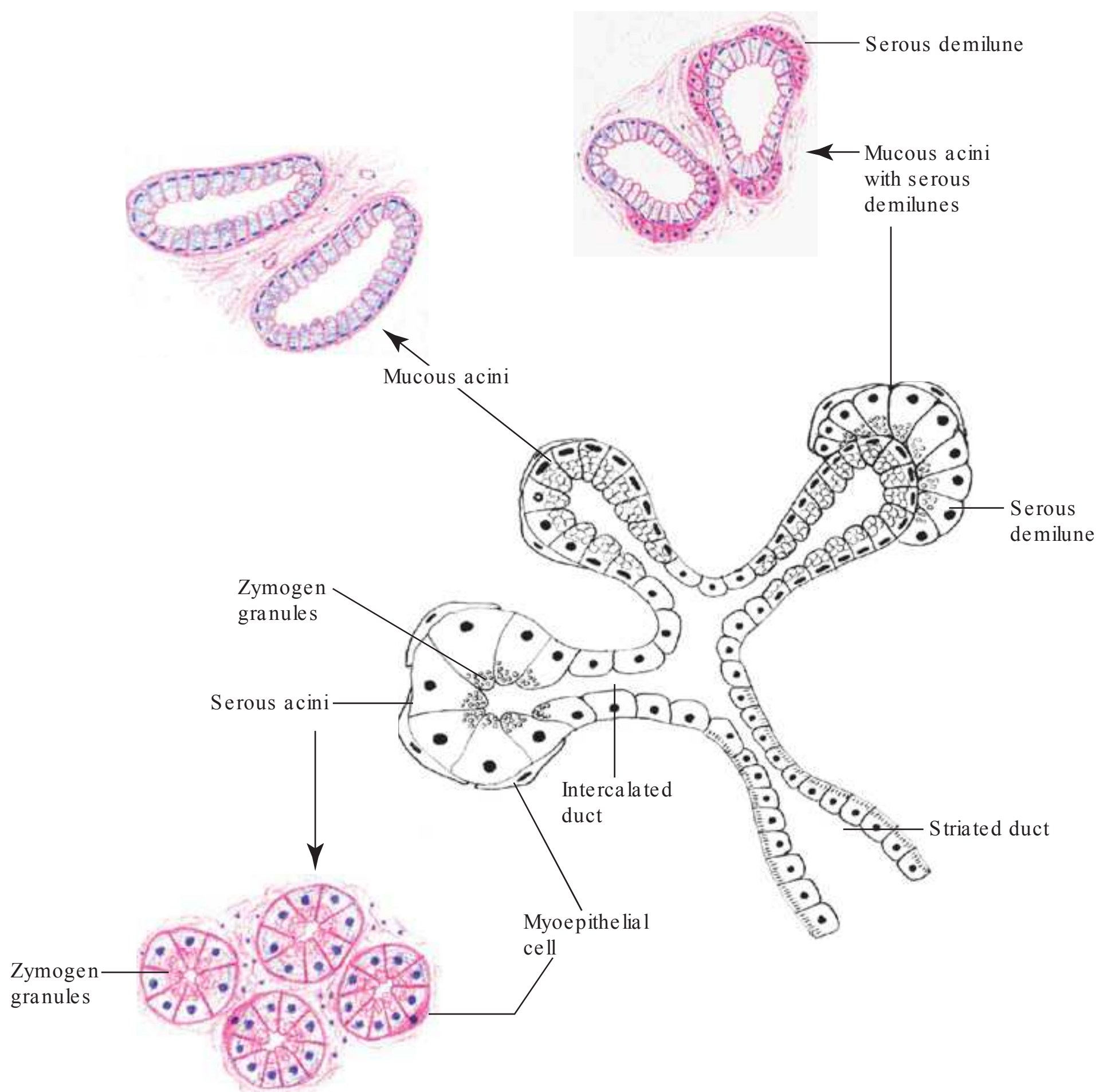
- The secretory part consists of branched tubuloacinar glands, containing two types of acini (singular: acinus): mucous and serous (Fig. 14.1).
- A salivary gland may have only one type of acini or may have both. The salivary gland having both types of acini is known as mixed or seromucous gland.

**1. Serous acini**

- Cells of serous acini are triangular in shape with round nuclei at their bases.
- Apical cytoplasm is eosinophilic due to the presence of eosinophilic granules called zymogen granules; cytoplasm at the base of each cell is basophilic (Fig. 14.1).
- The lumen of these acini is small.
- The secretion of serous acini is watery.

**2. Mucous acini**

- Cells in these acini are tall with flat nuclei at their bases (Fig. 14.1).
- These cells appear pale as the cytoplasm does not stain well, and hence these cells appear empty in H&E-stained sections.
- The lumen of these acini is larger than that of serous acini.
- The secretion of mucous acini is thick.



**Figure 14.1** Parenchyma and duct system of a salivary gland.



### Myoepithelial Cells

- Myoepithelial cells are spindle-shaped cells with oval nuclei.
- They are located within the basal lamina of the secretory acini and the ducts of the glands (Fig. 14.1).
- Contraction in these cells propels the secretions from the acini and the duct.

### Duct System

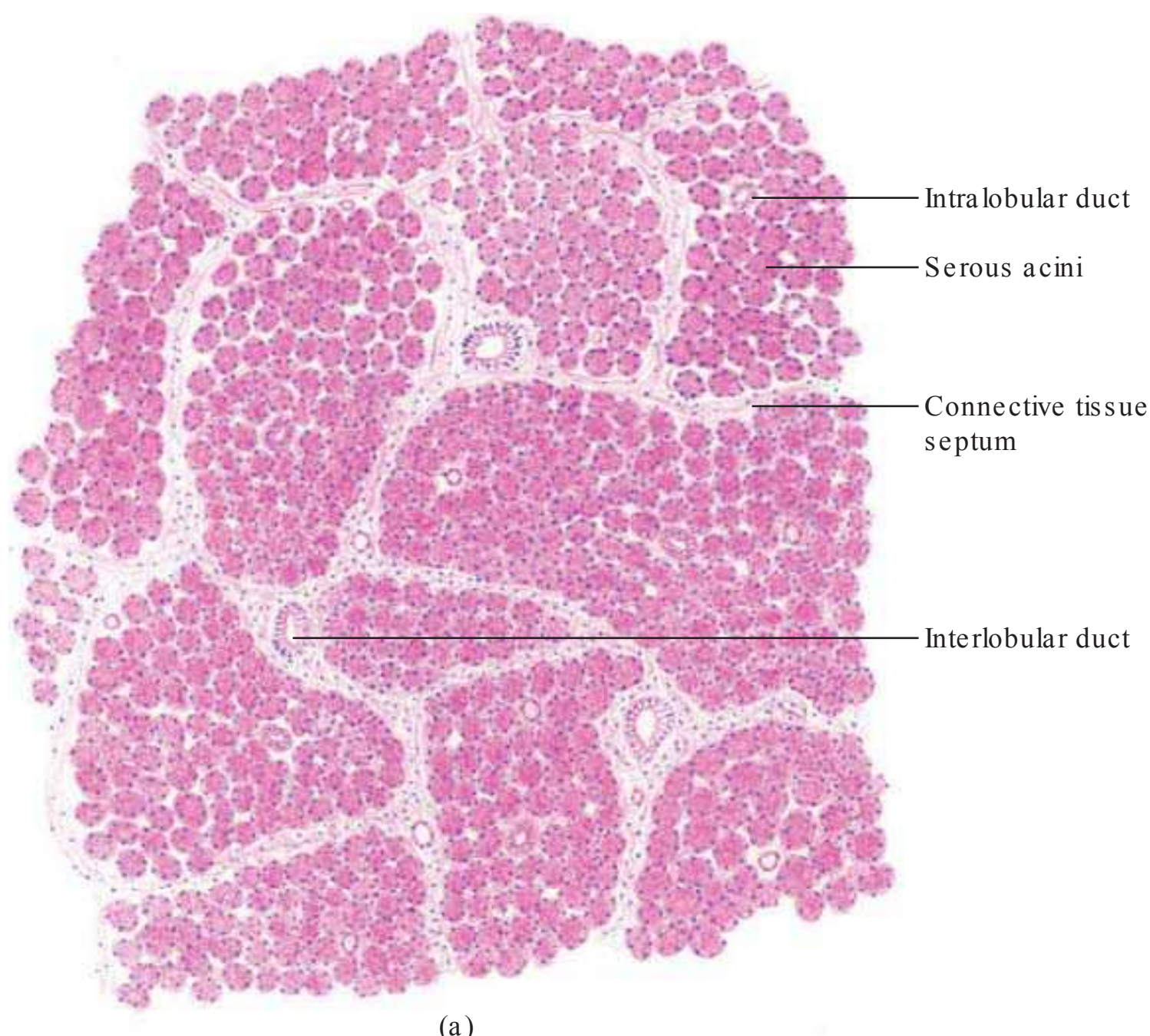
- The secretory acini drain into intercalated ducts and the intercalated ducts drain into larger ducts called striated ducts. Both intercalated and striated ducts are intralobular ducts (within the lobule of the gland).
- The striated duct drains into larger ducts located in connective tissue septa, the interlobular ducts. Interlobular ducts drain into the main duct which opens in the oral cavity. The location of these ducts is shown in Figure 14.2.
- Intercalated ducts are lined by simple cuboidal epithelium (Fig. 14.1). Striated ducts are also lined by simple cuboidal epithelium; however, these cells have striations at their bases (Fig. 14.1).
- Interlobular ducts at the beginning are lined by simple columnar epithelium. The epithelium changes to stratified columnar epithelium as the width of the duct increases. The terminal part of the main duct is lined by non-keratinised stratified squamous epithelium.

## MAJOR SALIVARY GLANDS

As mentioned earlier, there are three pairs of major salivary glands—the sublingual glands are located within the oral cavity, underneath the tongue, while the other two, parotid and submandibular, glands are situated outside the oral cavity. Refer to Figure 12.1, page 156 to see the location of these glands.

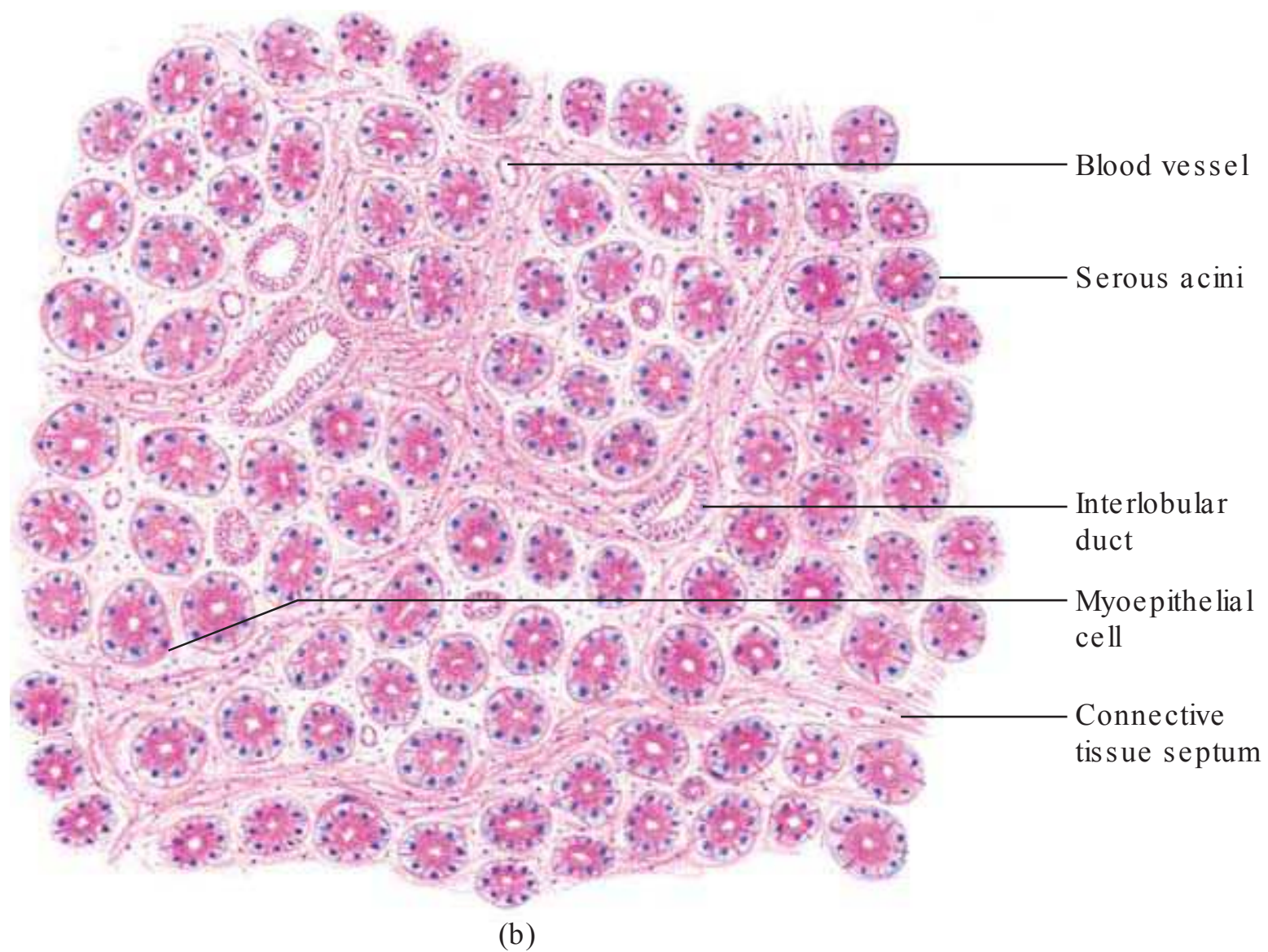
### Parotid Gland

The parotid gland is a serous salivary gland (Fig. 14.2; PMG 14.1).

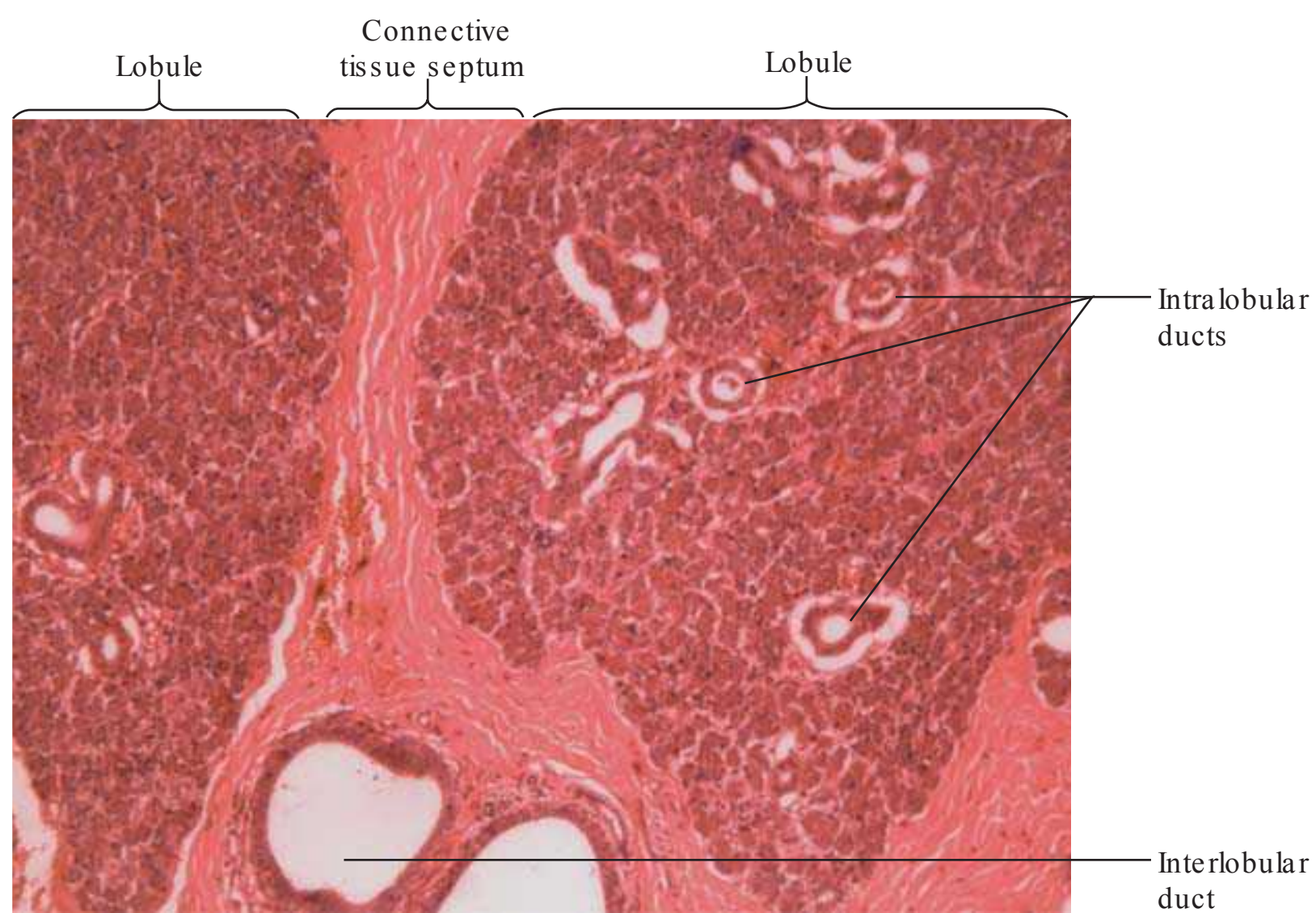


**Figure 14.2** (a) Section of parotid (serous) gland in low magnification (H&E pencil drawing). (continued)





**Figure 14.2** (continued) (b) Section of parotid (serous) gland in high magnification (H&E pencil drawing).

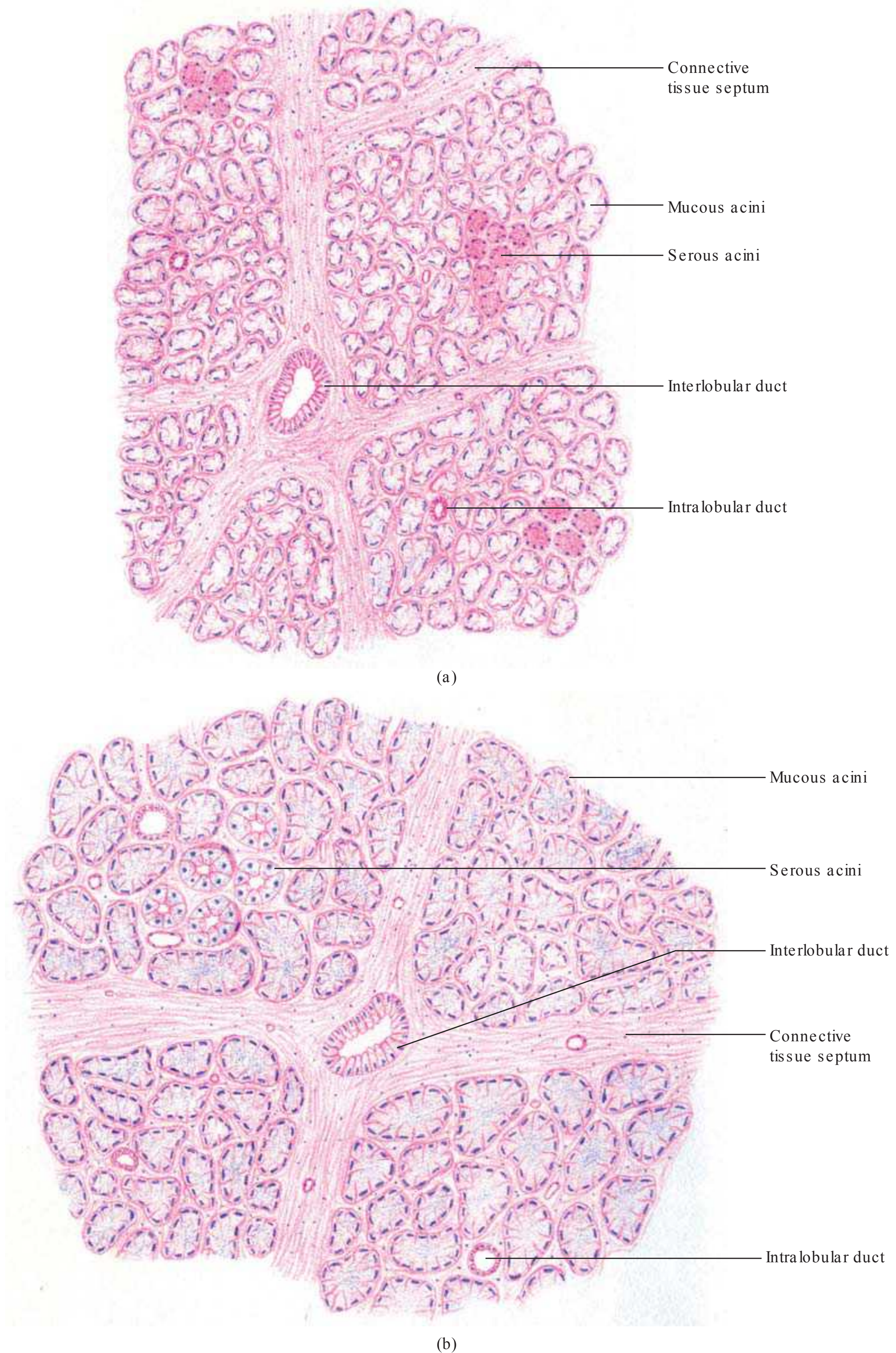


**PMG 14.1** Parotid (serous) gland (H&E stain, X10).

### Sublingual Gland

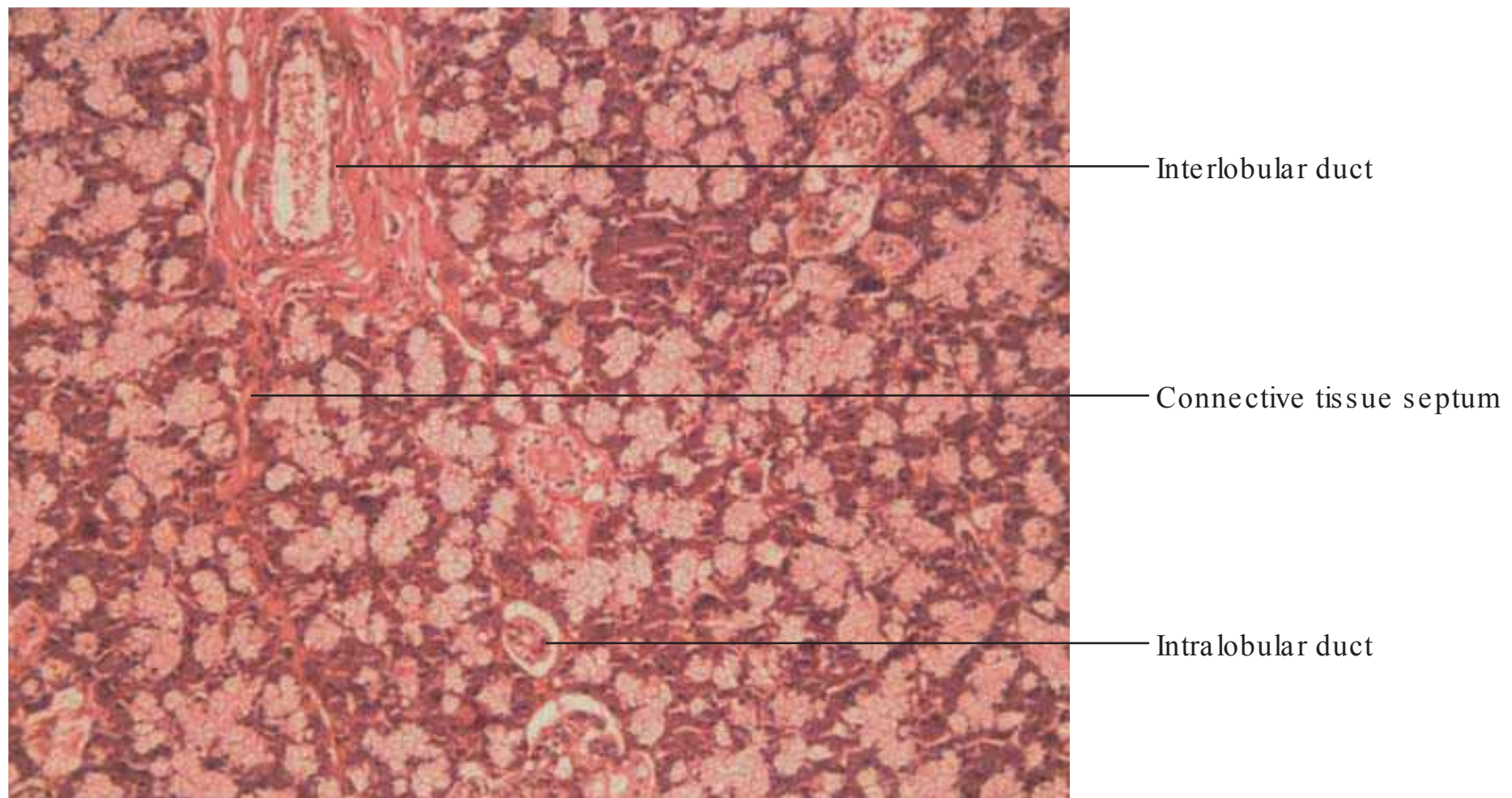
The sublingual gland is a mucous salivary gland; however, it also has very few serous acini (Fig. 14.3; PMG 14.2).





**Figure 14.3** Section of sublingual (mucous) salivary gland in (a) low magnification and (b) high magnification. Note the empty appearance of the mucous cells. (H&E pencil drawing)

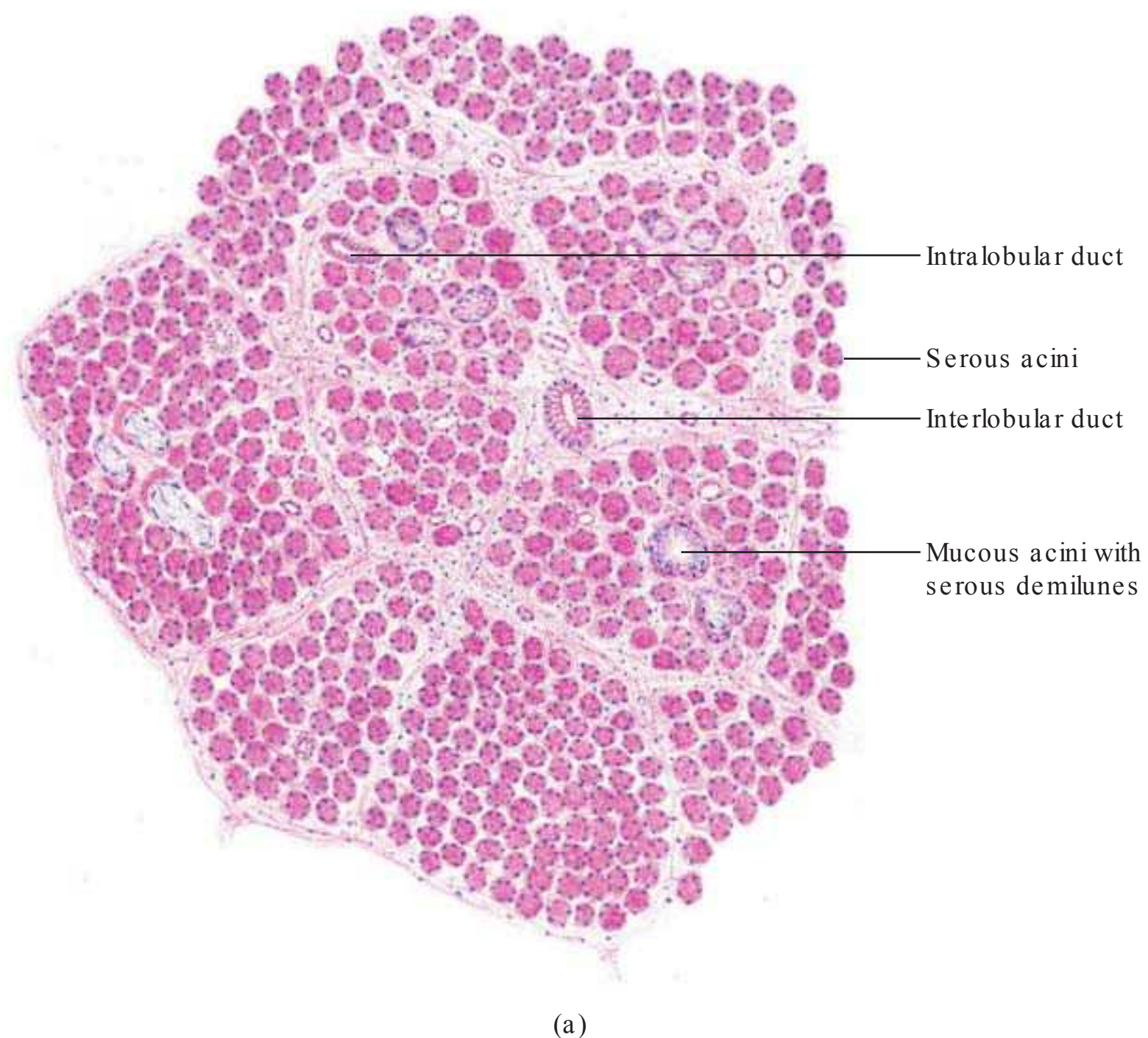




**PMG 14.2** Sublingual (mucous) salivary gland. Note the empty appearance of the mucous cells (H&E stain, X10).

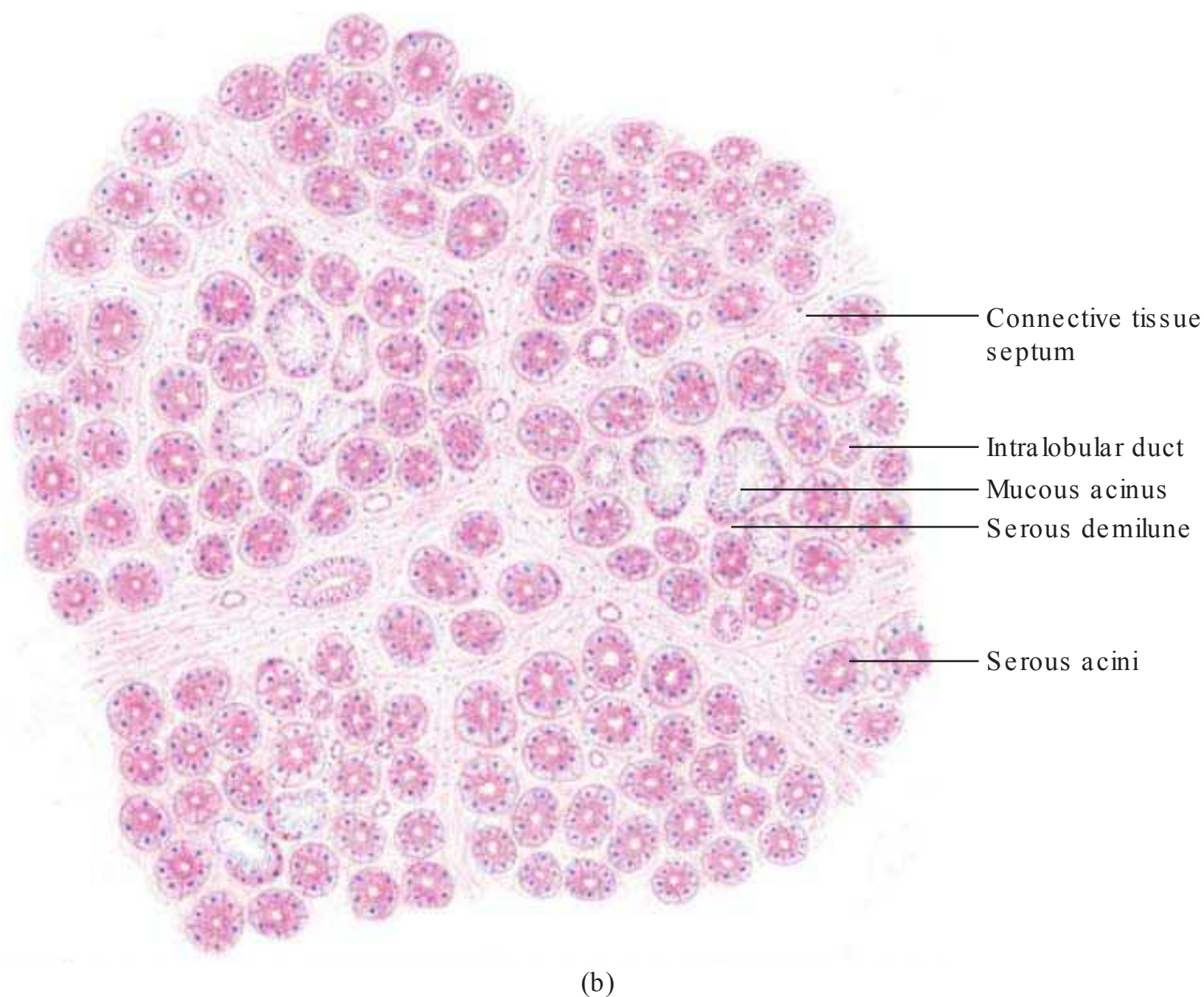
### Submandibular Gland

- The submandibular gland is a mixed salivary gland, predominantly serous with a few mucous acini.
- Some of mucous acini are capped with serous cells arranged as a half moon; hence, they are called serous demilunes (Fig. 14.4; PMG 14.3).

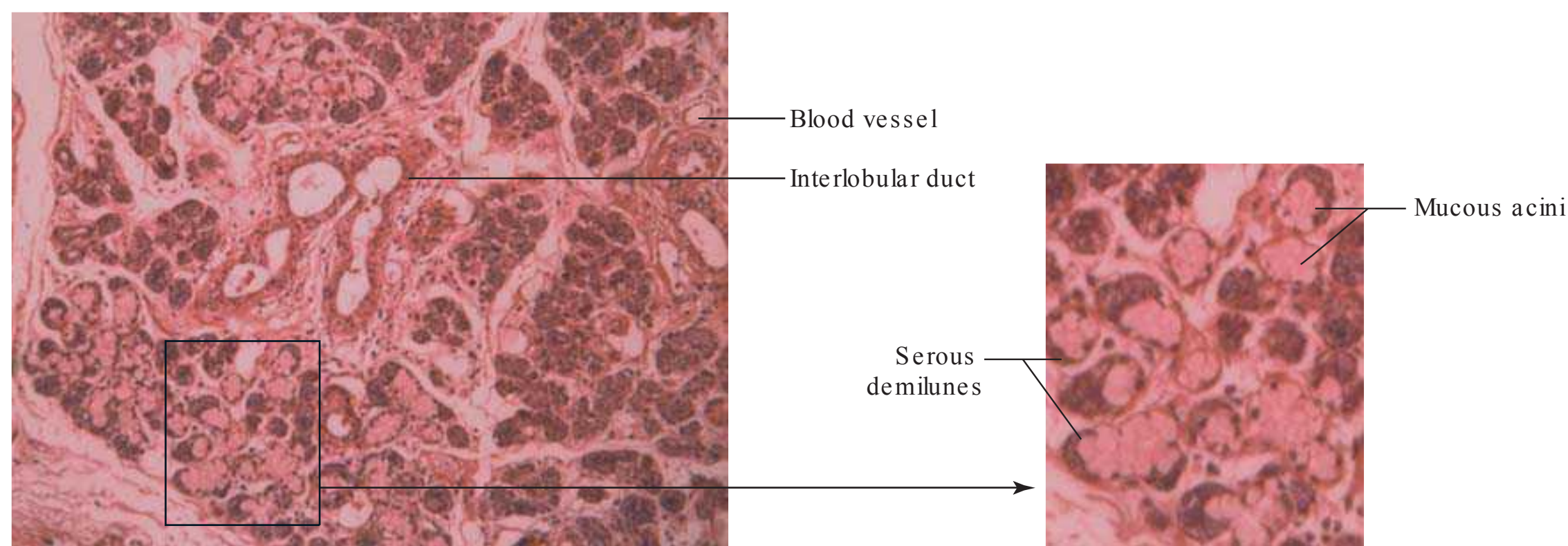


**Figure 14.4** (a) Section of the submandibular (mixed) salivary gland in low magnification (H&E pencil drawing). (continued)





**Figure 14.4** (continued) (b) Section of the submandibular (mixed) salivary gland in high magnification (H&E pencil drawing).

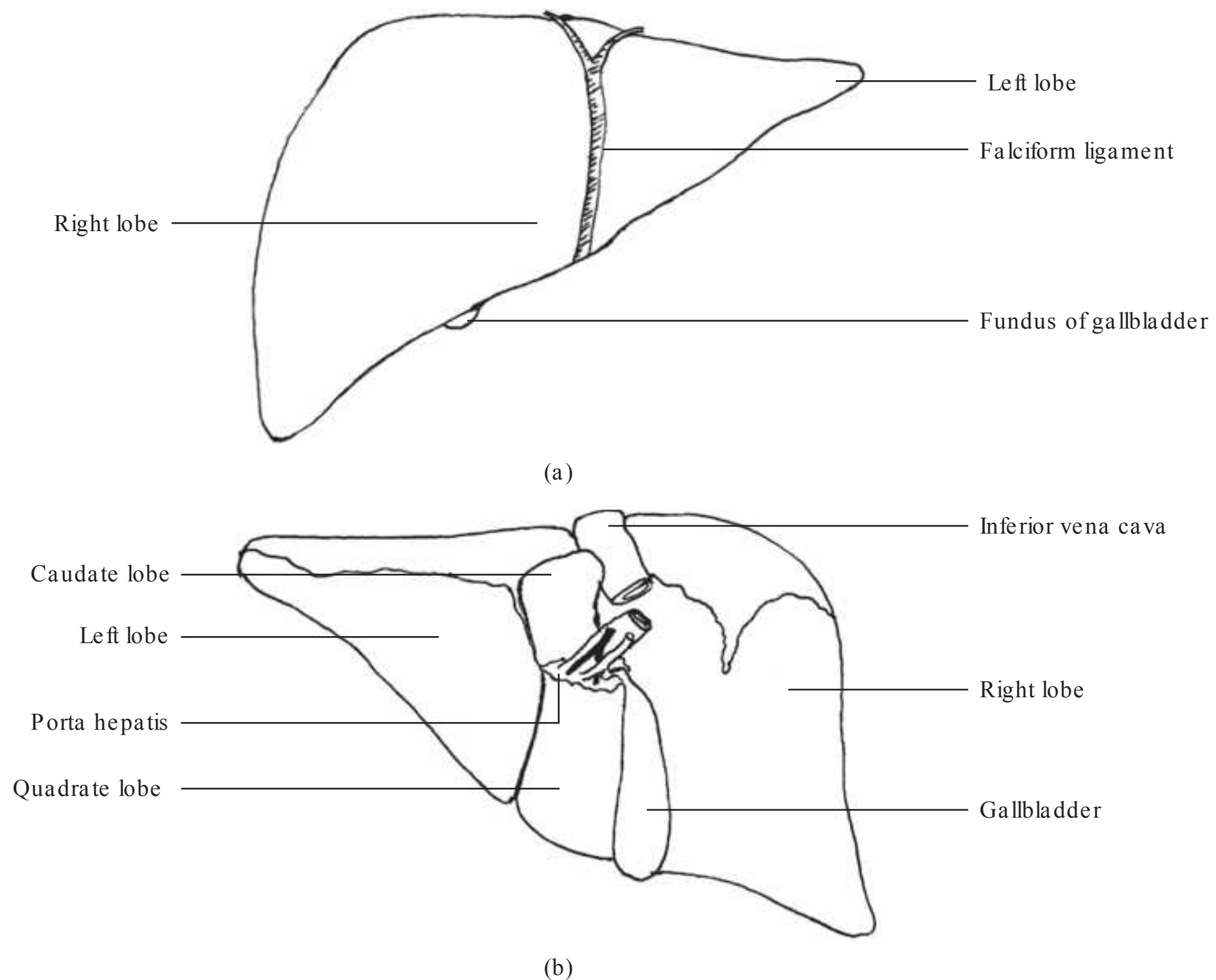


**PMG14.3** Section of submandibular (mixed) salivary gland (X10). Inset shows a further magnified view of submandibular gland. (H&E stain)



## LIVER

- The liver is the largest gland of the body.
- It is present under the diaphragm and occupies the entire right hypochondrium, part of epigastrium and left hypochondrium.
- Anatomically, it consists of four lobes: right, left, caudate and quadrate lobes. On the anterior surface right and left lobes separated by falciform ligament can be seen, while on the posteroinferior surface caudate and quadrate lobes are also present.
- The hilum or porta hepatis is present between the caudate and quadrate lobes. Many structures pass (enter and leave the liver) through the hilum. Structures entering the liver are right and left branches of the hepatic artery, portal vein and hepatic plexus of nerves, while structures leaving the liver are right and left hepatic ducts and lymphatics (Fig. 14.5).
- Functions: These include synthesis of urea, formation and secretion of bile, detoxification of metabolic wastes as well as many drugs, storage of glycogen, metabolism of cholesterol and fat, synthesis of plasma proteins and gluconeogenesis (i.e. conversion of lipids and amino acids into glucose).



**Figure 14.5** Diagram showing the lobes of liver: (a) anterior surface and (b) posteroinferior surface.

## MICROSCOPIC STRUCTURE

- The stroma of the liver consists of connective tissue capsule (Glisson's capsule).
- The parenchyma of the liver consists chiefly of the hepatocytes.

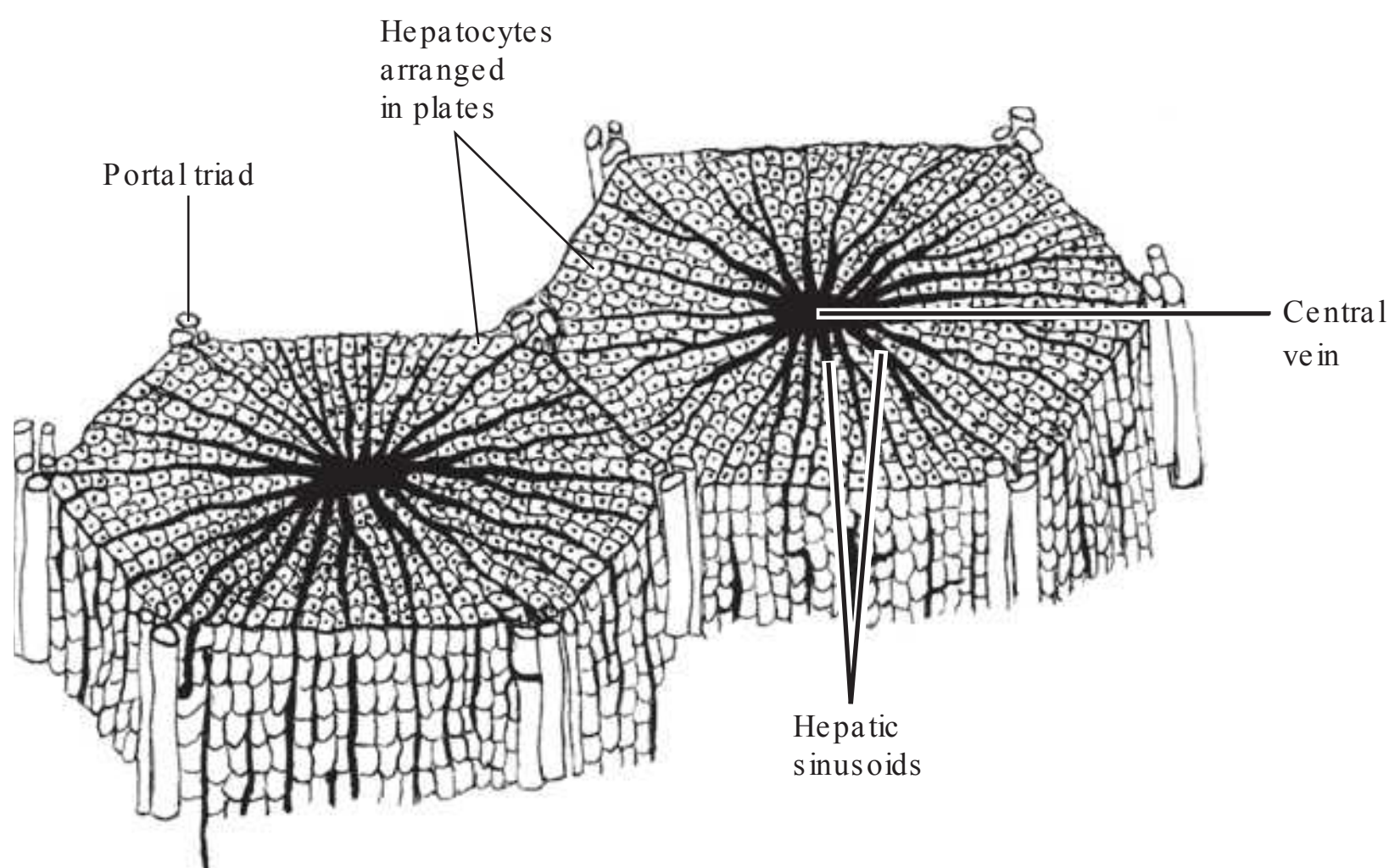


## Stroma

- Glisson's capsule covers the liver. It is made of connective tissue.
- At the hilum of the liver, the connective tissue of the capsule enters the parenchyma of the gland and branches extensively in various directions.
- As these branches of connective tissue penetrate the parenchyma, they carry the blood vessels along with them.
- The branches of connective tissue divide the parenchyma into the basic structural units of the liver, the 'classical' liver lobules or hepatic lobules.

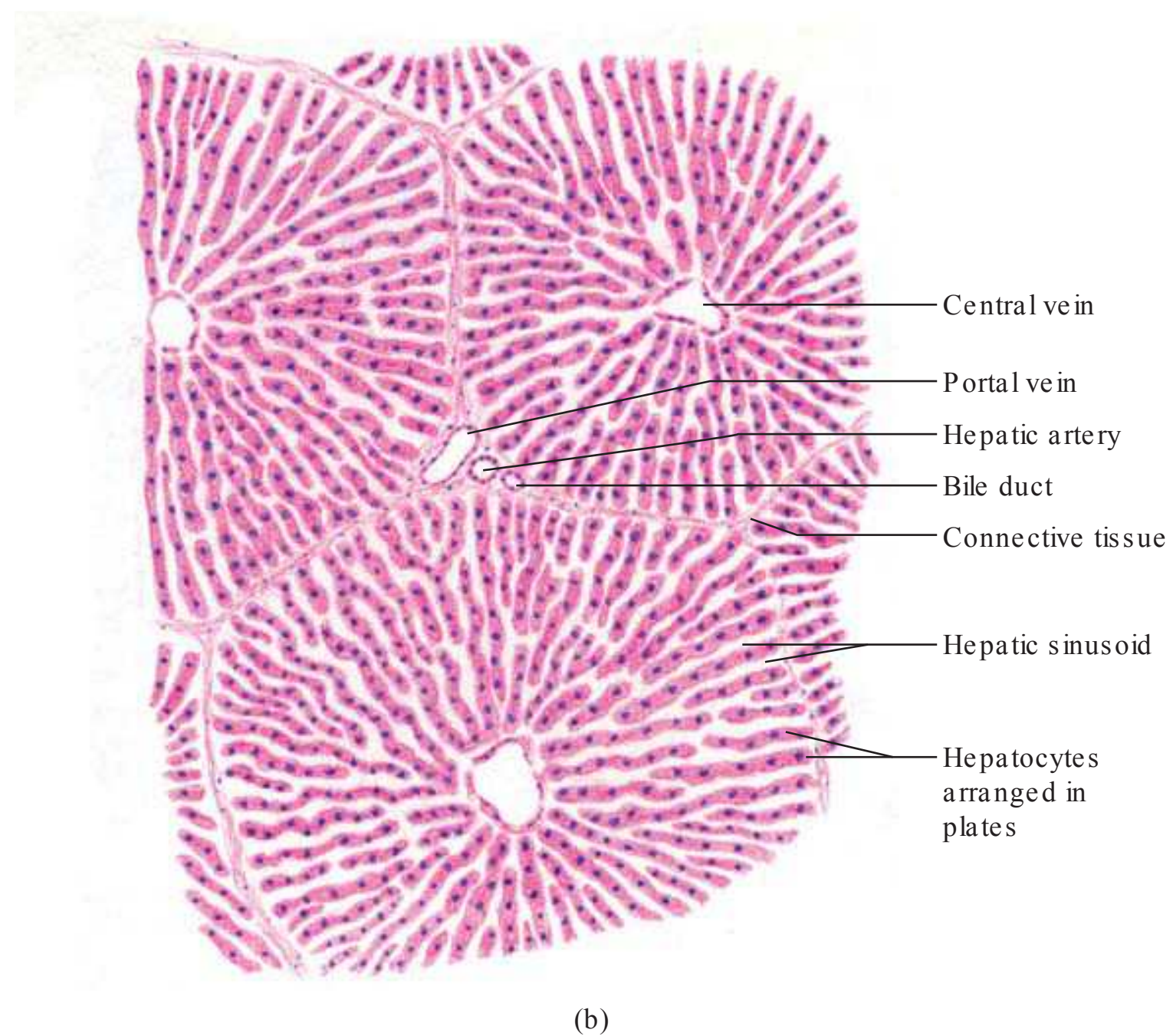
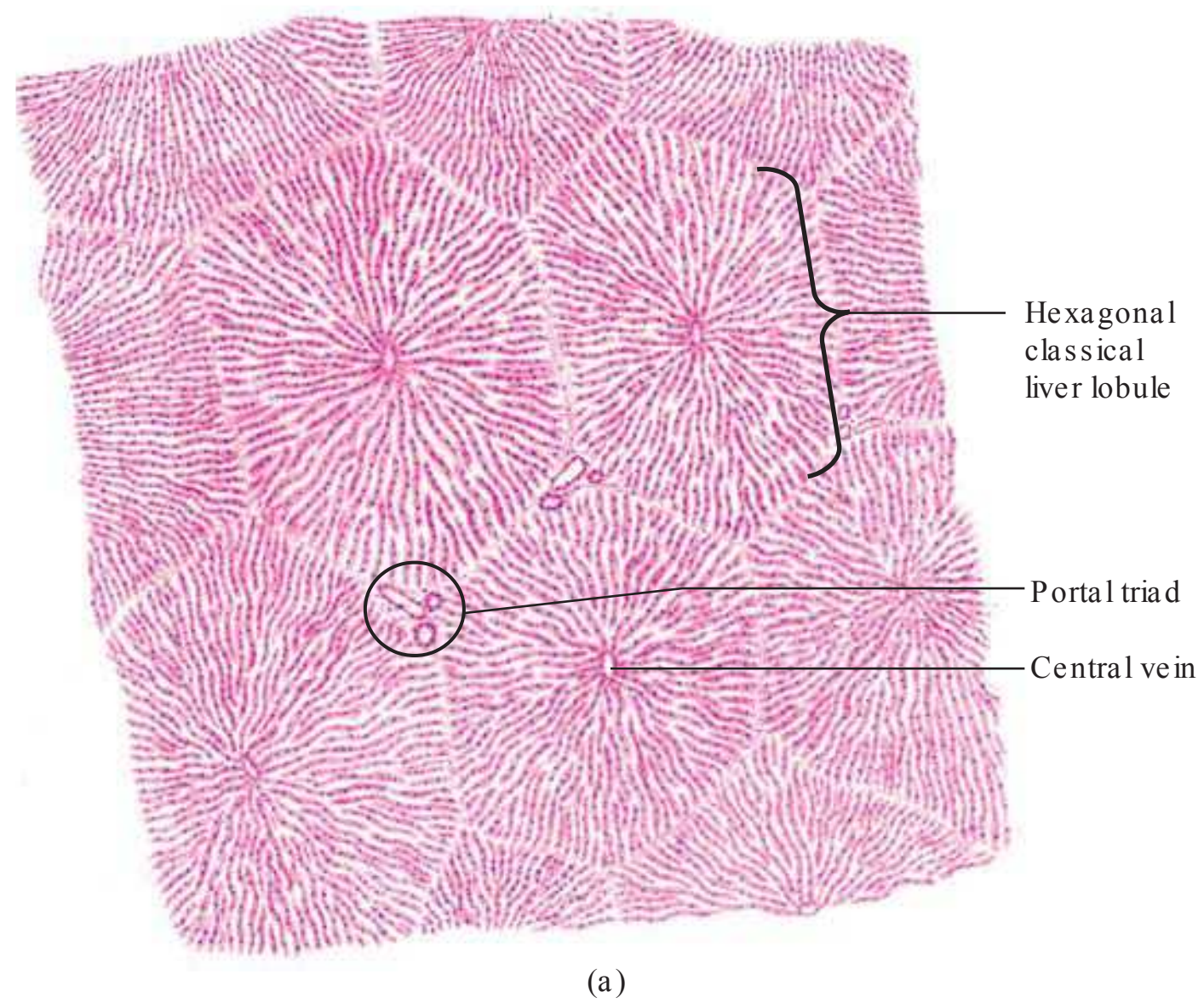
## Parenchyma

- Liver parenchyma can be divided into parenchymal units on three bases:
  - (a) Classical lobule, on structural basis: It is the basic structural unit of the liver.
  - (b) Portal lobule, on the basis of biliary flow through the liver (discussed later in the chapter).
  - (c) Hepatic acinus, on functional basis: It is the functional unit of the liver (discussed later in the chapter).
- The classical lobule is a part of parenchyma surrounded by connective tissue.
- It is hexagonal in shape. (The shape is not clearly seen in the human liver.)
- In the connective tissue, at the six angles of the lobules, there are portal triads (also called portal areas) which contain a branch of portal vein (the largest lumen in portal triad), a branch of hepatic artery, a bile duct and occasionally a lymphatic vessel (Figs 14.6 and 14.7; PMG 14.4). In the centre of each lobule is the central vein.
- The principal cell of the liver is a hepatocyte which is polyhedral in shape.
- Inside a hepatic lobule, hepatocytes are arranged in one- or two-cell thick plates (Fig. 14.6); these plates can be compared with a brick wall which is one or two bricks thick. In a brick wall, bricks are the building blocks, and in the plates of hepatocytes, hepatocytes are the building blocks. Neighbouring plates anastomose with each other and they are separated by hepatic sinusoids (Figs 14.6 and 14.7; PMG 14.5).
- In a hepatic lobule, these anastomosing plates of hepatocytes appear radiating from the central part of the lobule, all around the central vein.



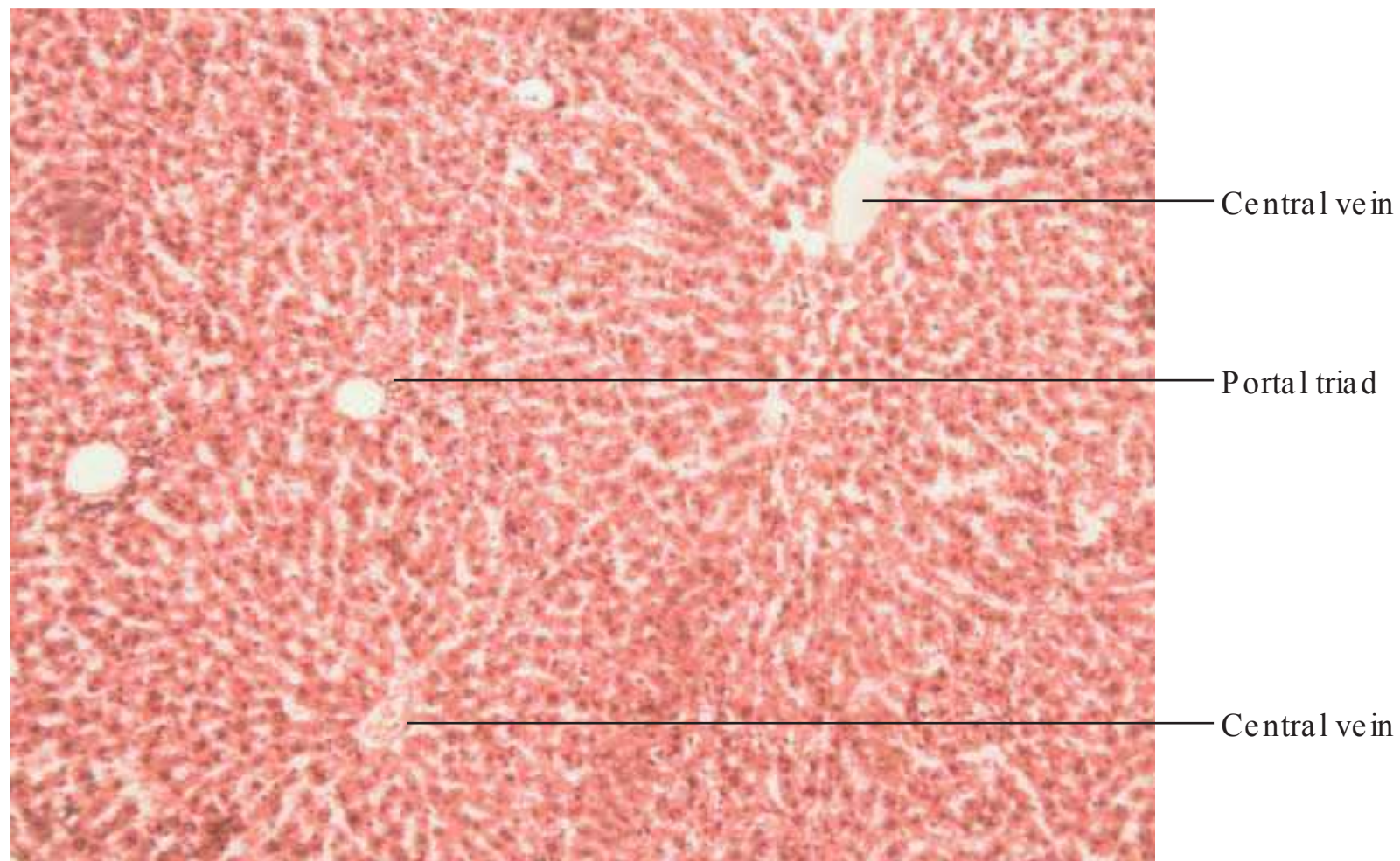
**Figure 14.6** Three-dimensional view of two classical lobules of liver. Each lobule is hexagonal in shape, portal triads are present at each angle and a central vein is present in the centre.



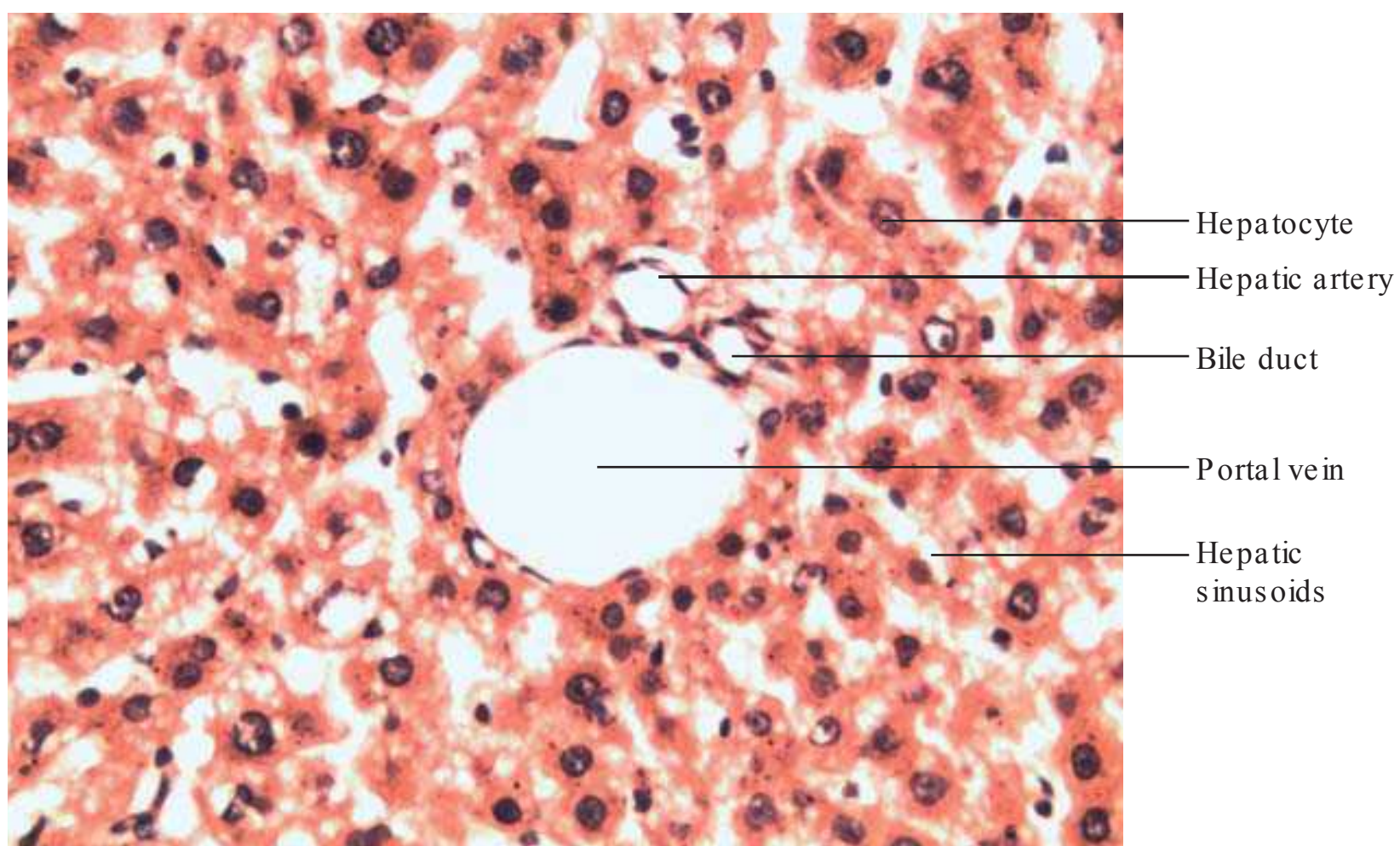


**Figure 14.7** Section of the liver in (a) low magnification and (b) high magnification. The classical lobule has been marked in (a). (H&E pencil drawing)





**PMG 14.4** Liver (H&Estain, X10).



**PMG 14.5** Portal triad (H&Estain, X40).

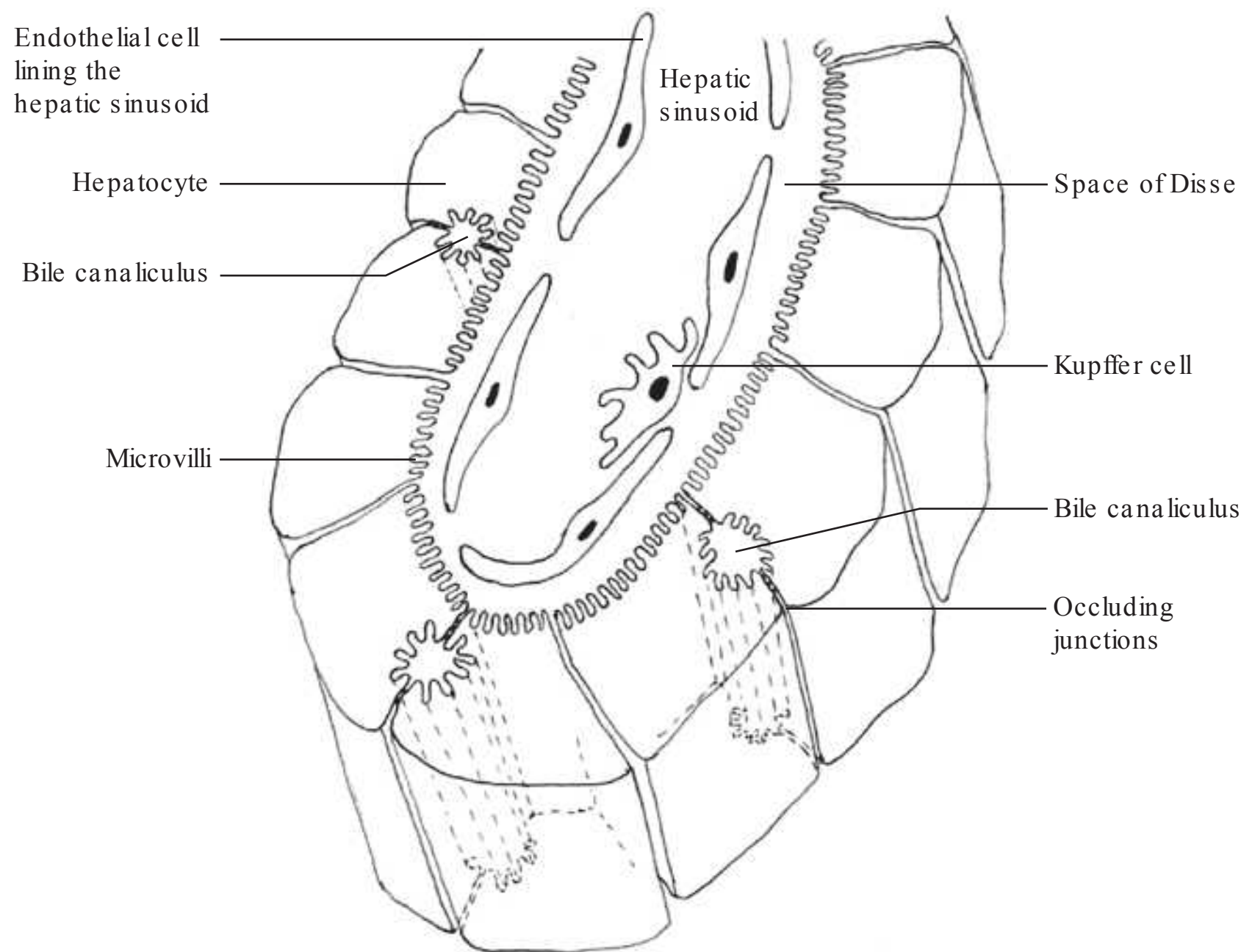
### Hepatic Sinusoids

- As the blood passes through the sinusoids, which are present in between the plates, the hepatocytes exchange metabolites from the blood.
- These sinusoids are lined by phagocytic cells, also called Kupfer cells, and endothelial cells (Fig. 14.8).
- These sinusoids are fenestrated. The lining endothelial cells are discontinuous and they lack basal lamina.
- There is a narrow space between the endothelial cells, lining the hepatic sinusoids, and the hepatocytes, and this space is called the space of Disse.

### Space of Disse

- The space of Disse is a narrow perisinusoidal space between the hepatocytes and the hepatic sinusoids (Fig. 14.8).



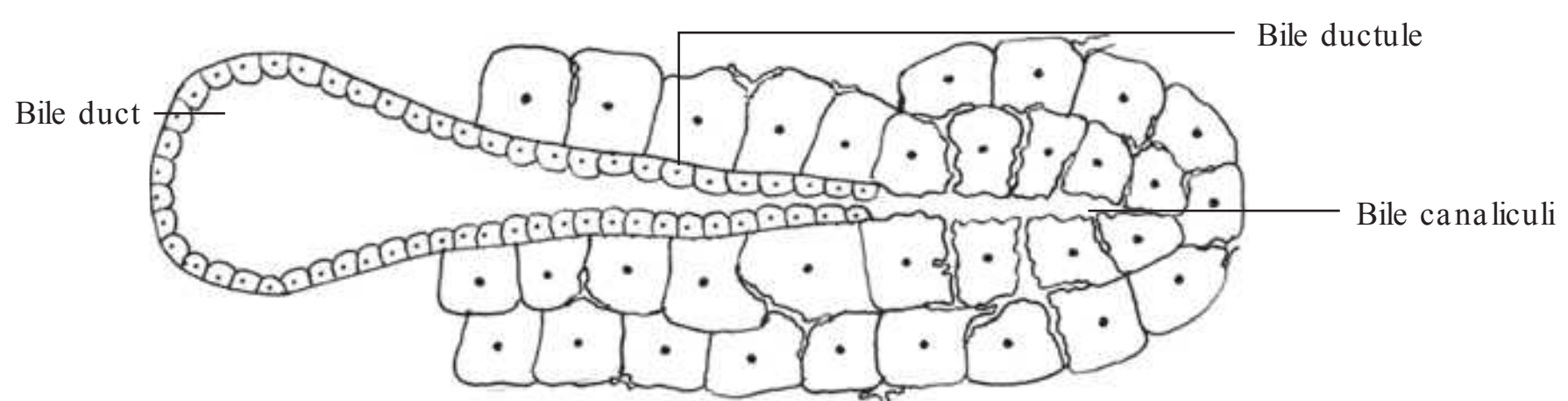


**Figure 14.8** Hepatic sinusoid, space of Disse and bile canaliculi.

- The exchange of substance between hepatocytes and blood takes place in the space of Disse.
- The surface of the hepatocytes that face the space of Disse bears numerous microvilli projecting into the space; these microvilli increase the surface area for absorption.

### Portal Lobule

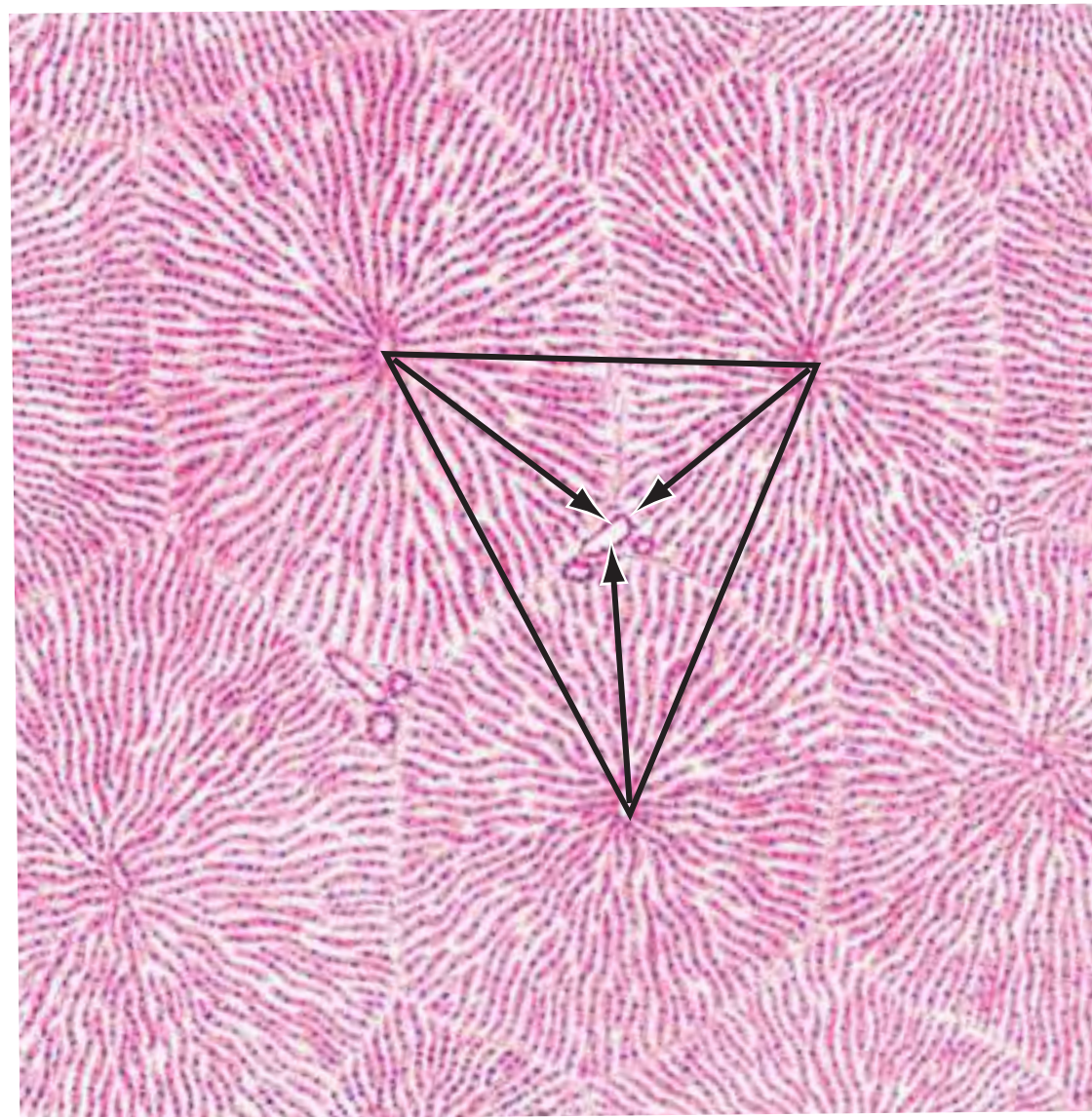
- This is another way of dividing the liver into parenchymal units. This is based on the direction of flow of the bile.
- Biliary tract—this is as follows:
  - Bile is formed by hepatocytes and secreted into bile canaliculi.
  - Bile canaliculi are tiny tubes, and the walls of these canaliculi are formed by the plasma membrane of the neighbouring hepatocytes (Figs 14.8 and 14.9). These canaliculi are sealed off from the surrounding intercellular space by the occluding junctions.
  - Bile canaliculi drain into bile ductules (also called canals of Hering) in the periphery of the hepatic lobule. Bile ductules are lined by a single layer of cuboidal cells (Fig. 14.9).
  - Bile ductules drain into bile ducts present in the portal triads.



**Figure 14.9** Biliary tract. Biliary canaliculi drain into bile ductules, and several bile ductules (only one is shown here) drain into one bile duct.



- Bile from the bile duct drains into larger ducts and finally into a single hepatic duct. This has been illustrated in Figure 14.13 (refer to Gross Anatomy textbooks for more detail).
- In the classical lobule, the direction of flow of bile is opposite to the direction of flow of blood in the sinusoids.
- The portal lobule is triangular in shape, with the portal triad in the centre and the central vein at each corner of the triangle (Fig. 14.10).
- The bile from all the hepatocytes present in this triangular unit gets collected in the bile duct present in the centre of the triangle.
- It should be noted that in classical lobule parenchyma surrounds the central vein whereas in portal lobule parenchyma surrounds the portal triad.

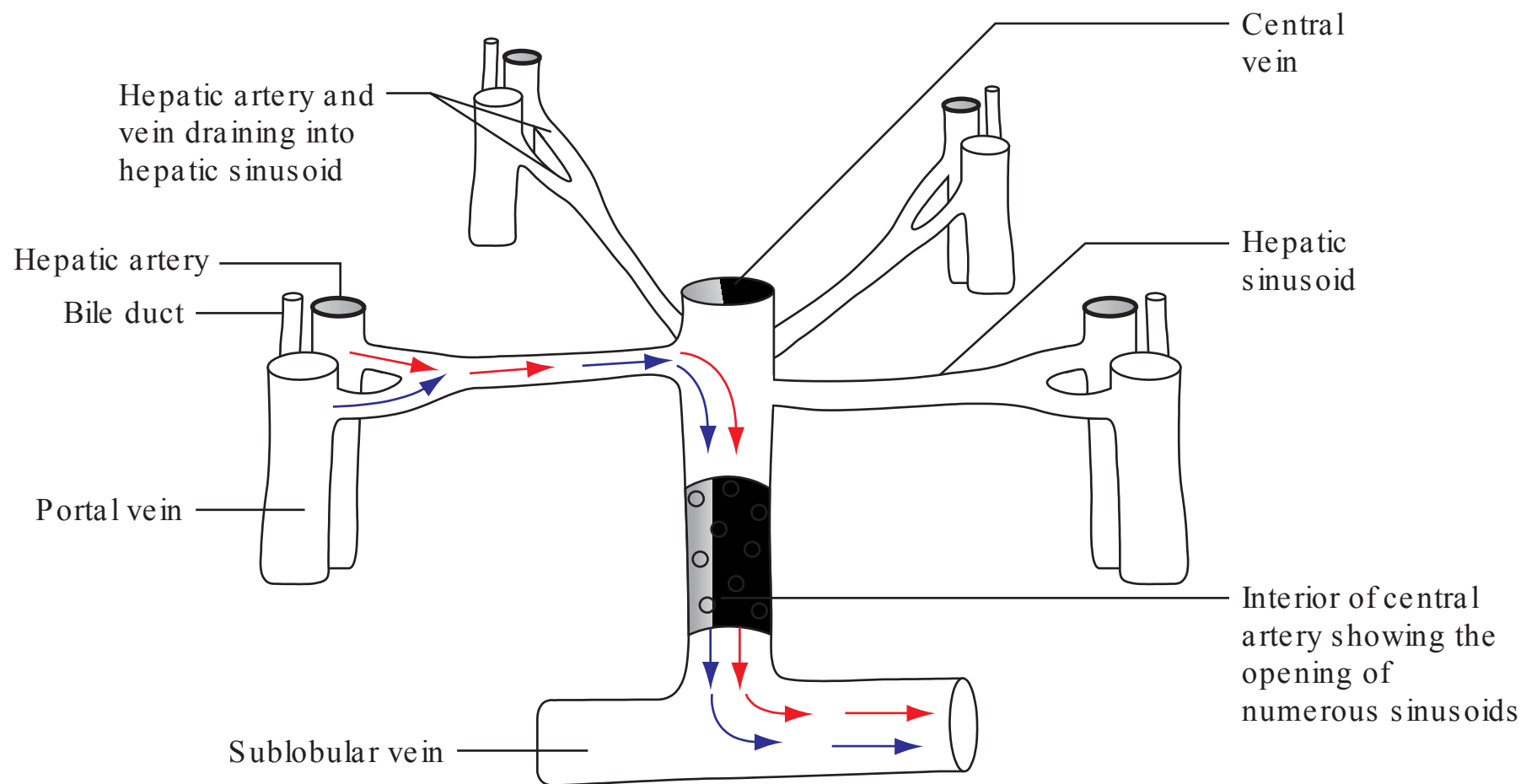


**Figure 14.10** Section of the liver in low magnification. The triangle shows a portal lobule. The portal triad is in the centre and central veins are at each corner of the triangle. Bile from all the hepatocytes present in this triangular unit gets collected in the bile duct present in the centre of the triangle. Arrows show the direction of bile flow.

### Hepatic Acinus

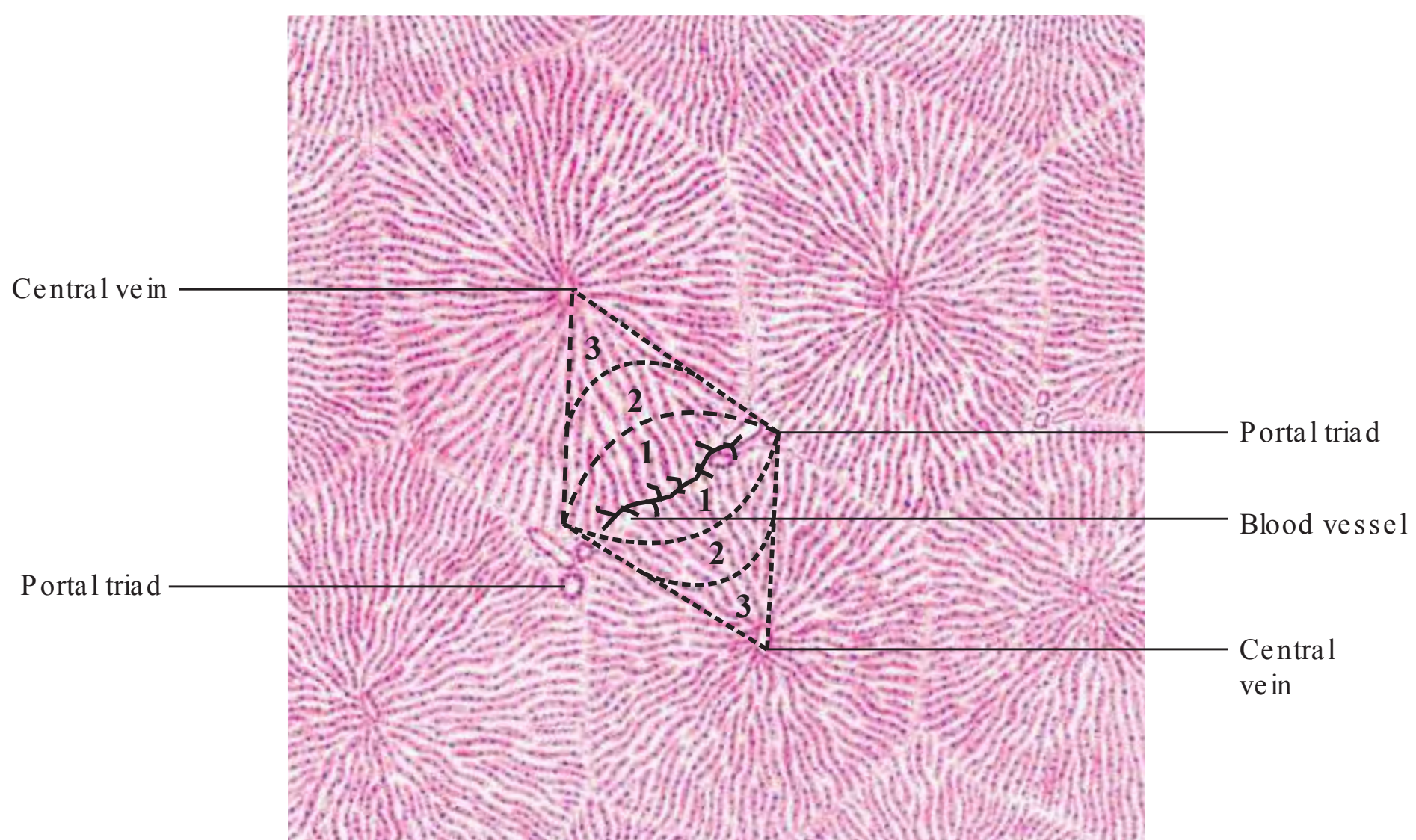
- Hepatic acinus is another way of dividing the liver into parenchymal units.
- It is also the functional unit of the liver. To understand the concept of hepatic acinus, it is important to first understand the blood supply of the liver.
- Blood supply of liver—this is as follows:
  - The liver gets its blood supply from two sources—the hepatic artery and the portal vein. The hepatic artery brings oxygenated blood; it provides about 20–25% of the blood to the liver. The portal vein brings nutrient-rich blood from the intestine and breakdown products of haemoglobin from the spleen to the liver; it provides about 75–80% of the blood to the liver.
  - Both these vessels enter the liver through porta hepatis; lying within the connective tissue, they divide as the connective tissue divides in the liver parenchyma.
  - In the classical lobule, they are present at the angles of the lobule in the portal triad.
  - From the portal triad, blood is delivered into the hepatic sinusoids and from the sinusoids to the central vein (Fig. 14.11).
  - The central vein drains into larger sublobular vein, which drains into the hepatic vein.





**Figure 14.11** Hepatic circulation (red arrows for arterial and blue arrows for venous blood). Blood from the hepatic artery and the portal vein is delivered into hepatic sinusoids, and from here the blood reaches the central vein. The central vein drains into the larger sublobular vein, which drains into the hepatic vein (not shown here).

- Hepatic acinus is diamond shaped, and in the middle of this unit lies the branches of the blood vessels present in the portal triad. Blood from these branches is delivered into the sinuses of the adjacent classical lobules. The hepatocytes and the sinuses (of the adjacent classical lobule) around these blood vessels contribute to the acinus (Fig. 14.12).
- At the two opposite angles of the diamond-shaped acinus are central veins and at the other two opposite angles are the portal triads.
- The acinus is divided into three zones according to the distance from the blood supply:
  - (a) Zone I hepatocytes are closest to blood vessels and they are best oxygenated.
  - (b) Zone II is less oxygenated than Zone I.
  - (c) Zone III which is farthest from blood vessels (near the central vein) has the poorest oxygen supply.

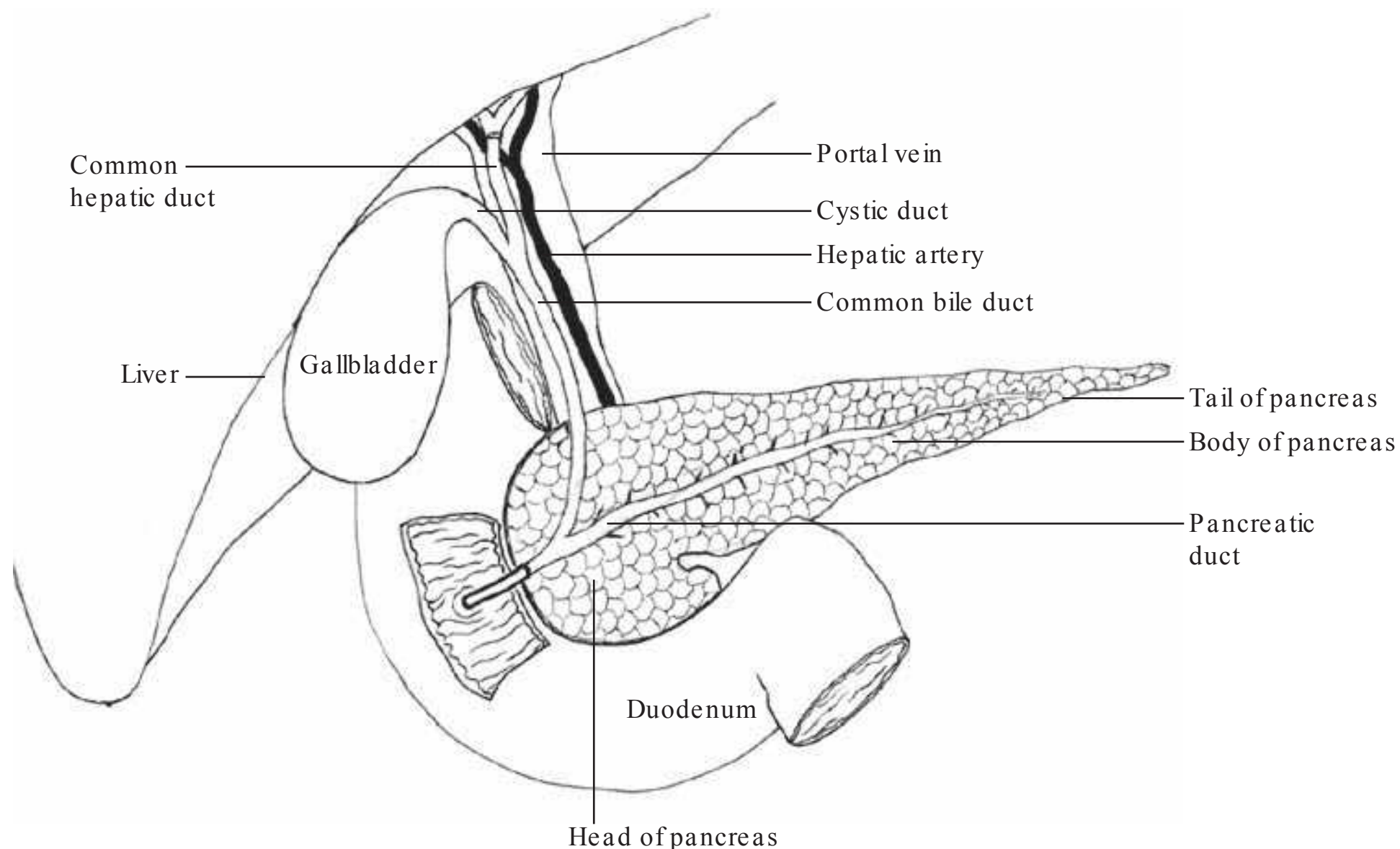


**Figure 14.12** Hepatic acinus. 1, Zone I; 2, Zone II; 3, Zone III.



## PANCREAS

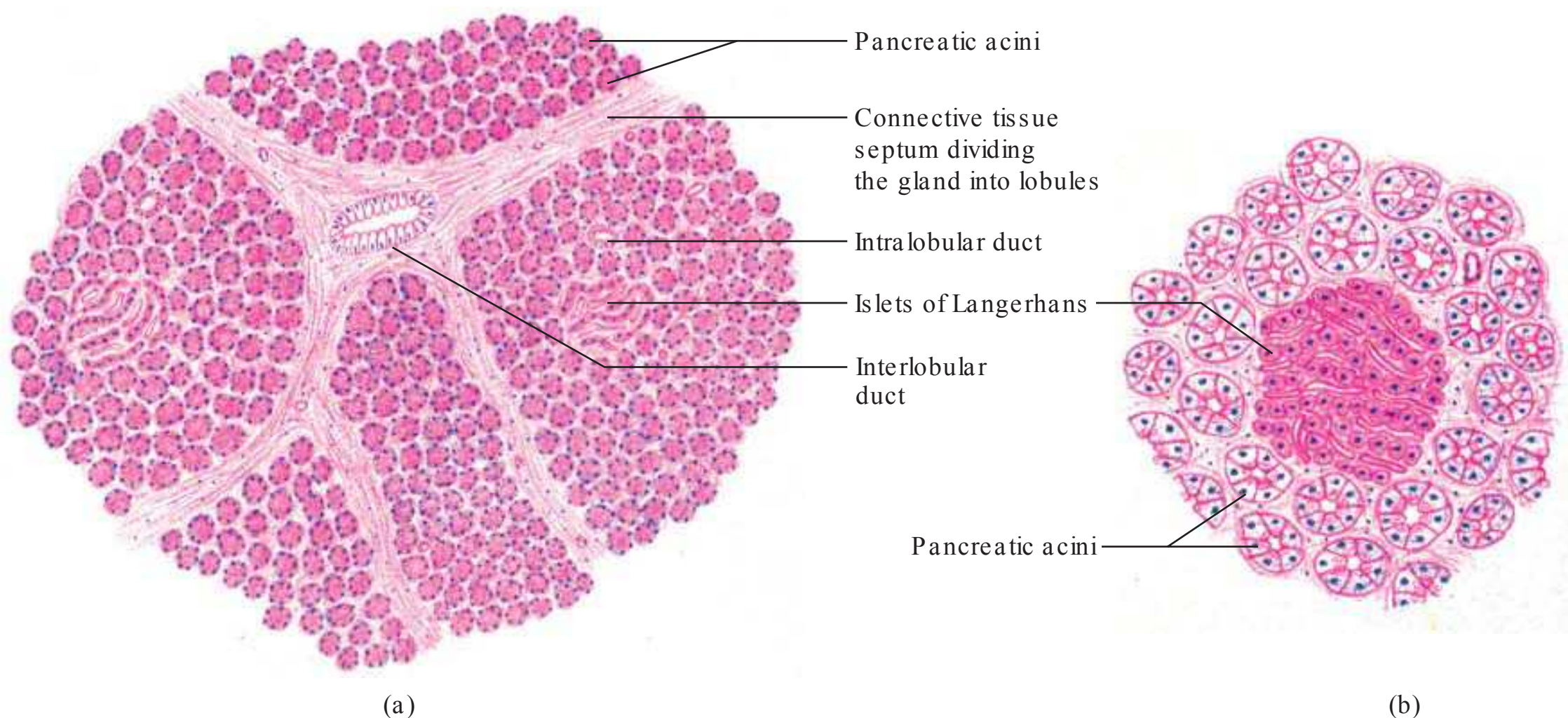
Pancreas is a retroperitoneal organ; it extends from the concavity of the duodenum to the hilum of the spleen. It consists of (from right to left) a head located within the concavity of the duodenum, a neck which is a constricted part, a body which forms the major bulk of the gland and a tail which is related to the hilum of the spleen (Fig. 14.13).



**Figure 14.13** Pancreas, gallbladder, extrahepatic biliary tract and structures passing through the porta hepatis.

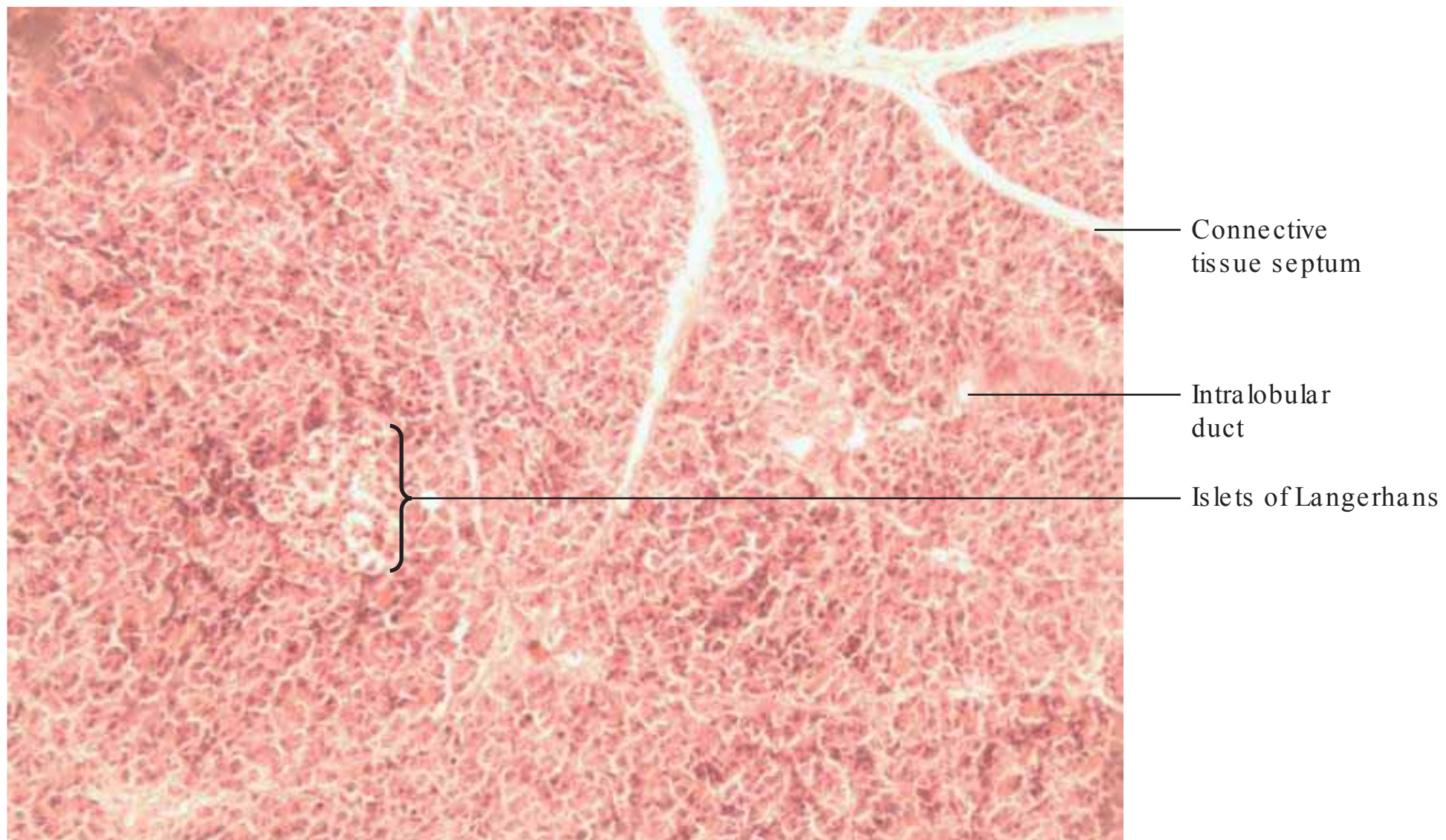
### MICROSCOPIC FEATURES (Fig. 14.14; PMG 14.6)

The pancreas has three components: stroma, parenchyma and a duct system. The parenchyma has exocrine and endocrine parts. The duct system carries the secretion of the exocrine part into the duodenum.



**Figure 14.14** Section of pancreas in (a) low and (b) high magnification. In the islets of Langerhans, cells arranged in irregular cords and capillaries in between the cords can be seen. (H&E pencil drawing)





**PMG 14.6** Pancreas (H&E stain, X10).

### Stroma

The gland is covered with a thin capsule of connective tissue. From this capsule numerous septa arise which divide the parenchyma of the gland into lobules (PMG 14.6).

### Exocrine Part and Duct System

The exocrine part consists of compound acinar glands.

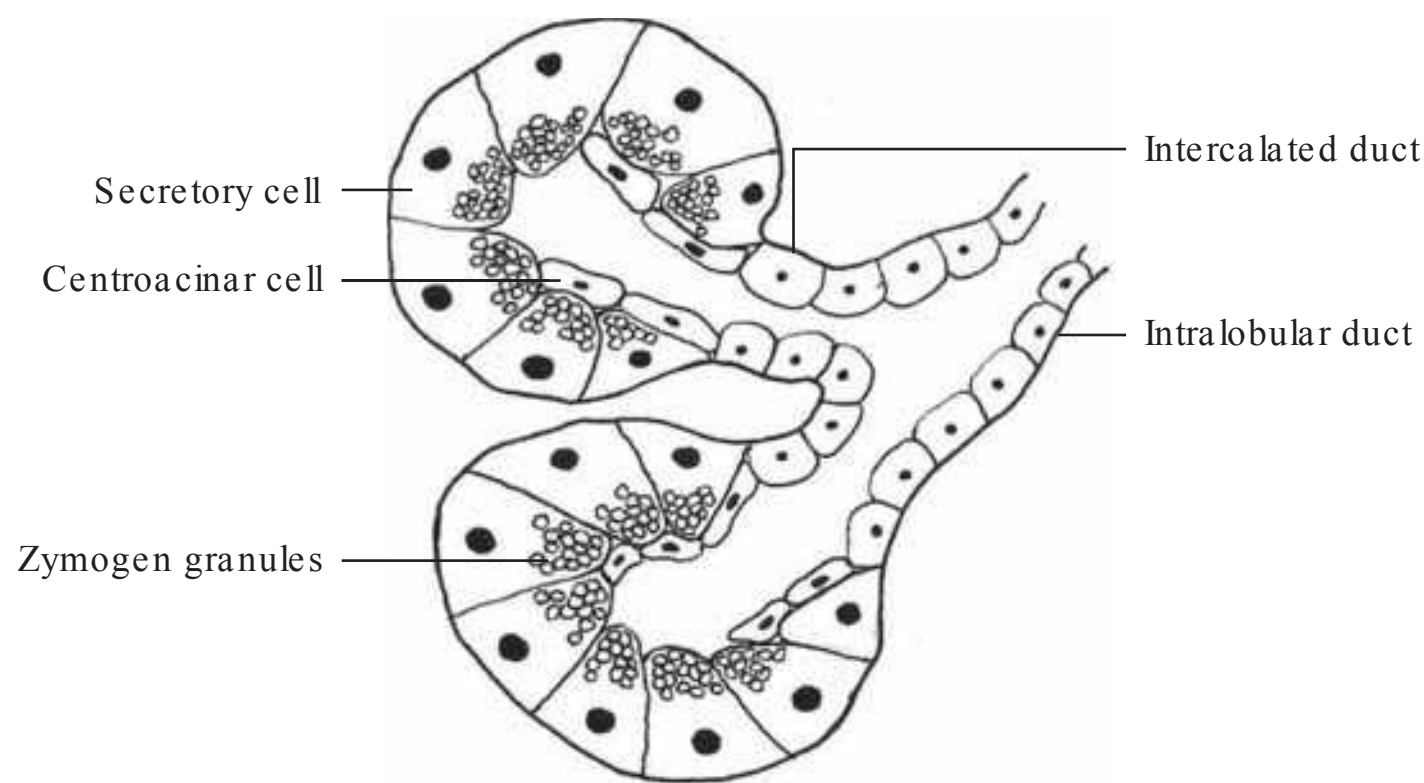
#### *Pancreatic Acini*

- The acini of pancreas resemble the acini of parotid glands and consist of a group of pyramid-shaped acinar cells arranged around a small lumen. Secretions of these cells drain into this lumen (Fig. 14.14).
- These cells have round nuclei at their bases.
- The cytoplasm in the basal portion of the cell is basophilic.
- The cytoplasm in the apical portion of the cell has eosinophilic zymogen granules containing digestive enzymes.

#### *Duct System*

- The duct system begins within the acini; the initial part of the duct is known as intercalated duct. The part of the intercalated duct inside the acini is lined by centroacinar cells (Fig. 14.15).
- These ducts drain into intercalated ducts which drain into intralobular ducts located within a lobule. Intralobular ducts drain into large interlobular ducts which are present in the connective tissue septum separating the adjacent lobules (Fig. 14.14; PMG 14.6), and finally, into the main pancreatic duct which opens into the second part of the duodenum along with the bile duct.
- Smaller ducts (intralobular) are lined by simple cuboidal epithelium and larger ducts (interlobular) by columnar epithelium.





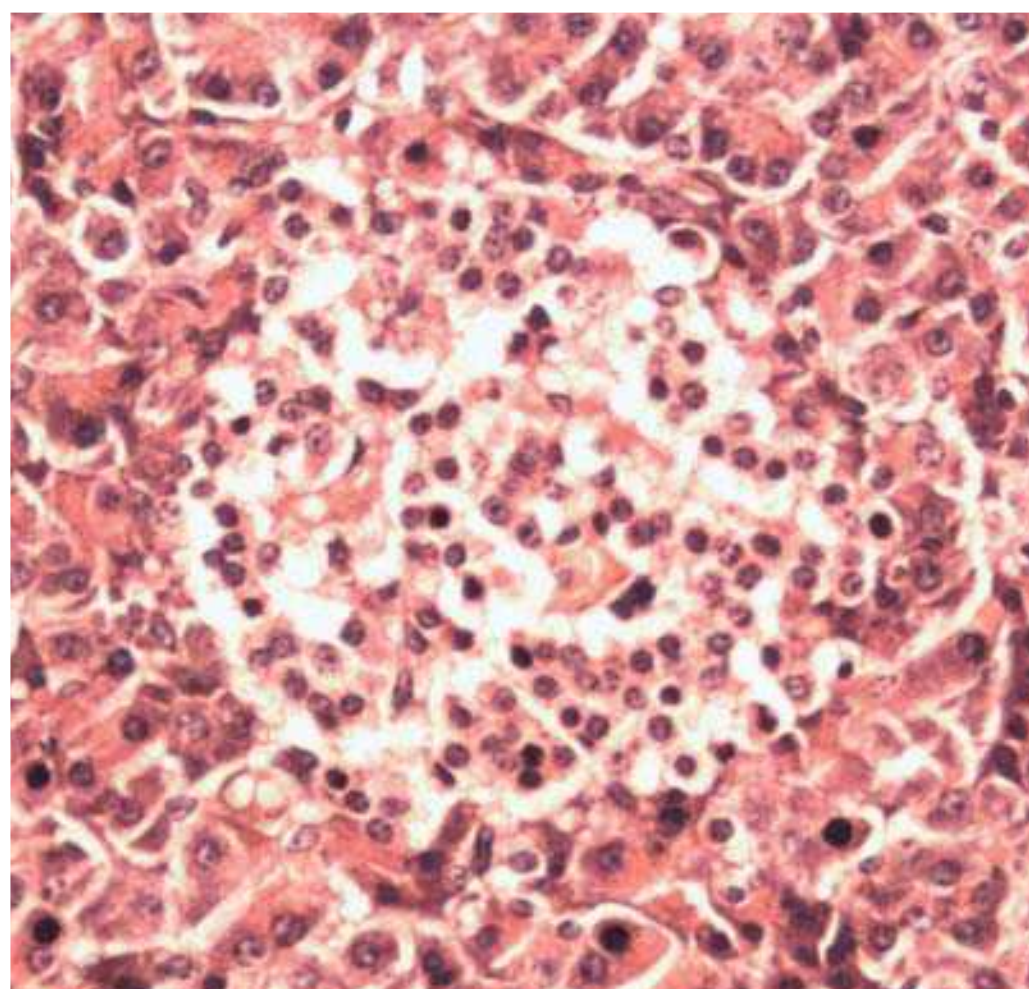
**Figure 14.15** Exocrine part of pancreas. Pyramid-shaped acinar cells are arranged in groups to form secretory acini. Zymogen granules are present in the apical part of acinar cells. Centroacinar cells are present within the acini where the duct system begins.

### *Centroacinar Cells*

- Centroacinar cells are seen at the centre of the acini where the duct system begins (Fig. 14.15).
- They have a central nucleus and pale cytoplasm.
- They add bicarbonate ions to the pancreatic juice, which neutralise the acidic contents entering the duodenum from the stomach.

### **Endocrine Part**

- Islets of Langerhans constitute the endocrine part, and they are scattered throughout the exocrine part, most abundantly in the tail region.
- These islets consist of polyhedral cells, arranged in irregular cords (Fig. 14.14; PMG 14.6 and 14.7). In between the cords there are capillaries; secretions of the endocrine cells are drained into these capillaries.



**PMG 14.7** Islets of Langerhans (H&E stain, X20).

- Islets of Langerhans have four types of cells: alpha, beta, delta and PP cells.
- Majority of the beta cells are located in the centre of the islets; alpha and delta cells are in the periphery and PP cells are found throughout the islets. These cells can be demonstrated by immunocytochemical method.

(The microscopic structure of pancreas resembles parotid glands; look for islets of Langerhans.)

### **PANCREATIC SECRETIONS**

Secretions of both the exocrine and endocrine parts of pancreas are discussed below.

#### **Exocrine Part**

- The main components of the secretions of the exocrine part are fluid rich in bicarbonate ions and digestive enzymes.
- Bicarbonate ions make the secretions alkaline and they (along with bile juice) neutralise the acidic chyme.
- These secretions are under hormonal control, secretin and cholecystokinin being the principal hormones.

#### **Endocrine Part**

Secretions of the endocrine part and their effects are mentioned in Table 14.1.

**Table 14.1** Cell Types of Islets of Langerhans

Type of cell	Percentage in islets of Langerhans	Secretion	Effect of the secretion
Alpha	20	Glucagon	Rise in blood glucose level
Beta	70–75	Insulin	Decrease in blood glucose level
Delta	5–8	Somatostatin	Inhibition of the secretion of nearby alpha and beta cells
PP	1	Pancreatic peptide	Inhibition of exocrine secretions of the pancreas

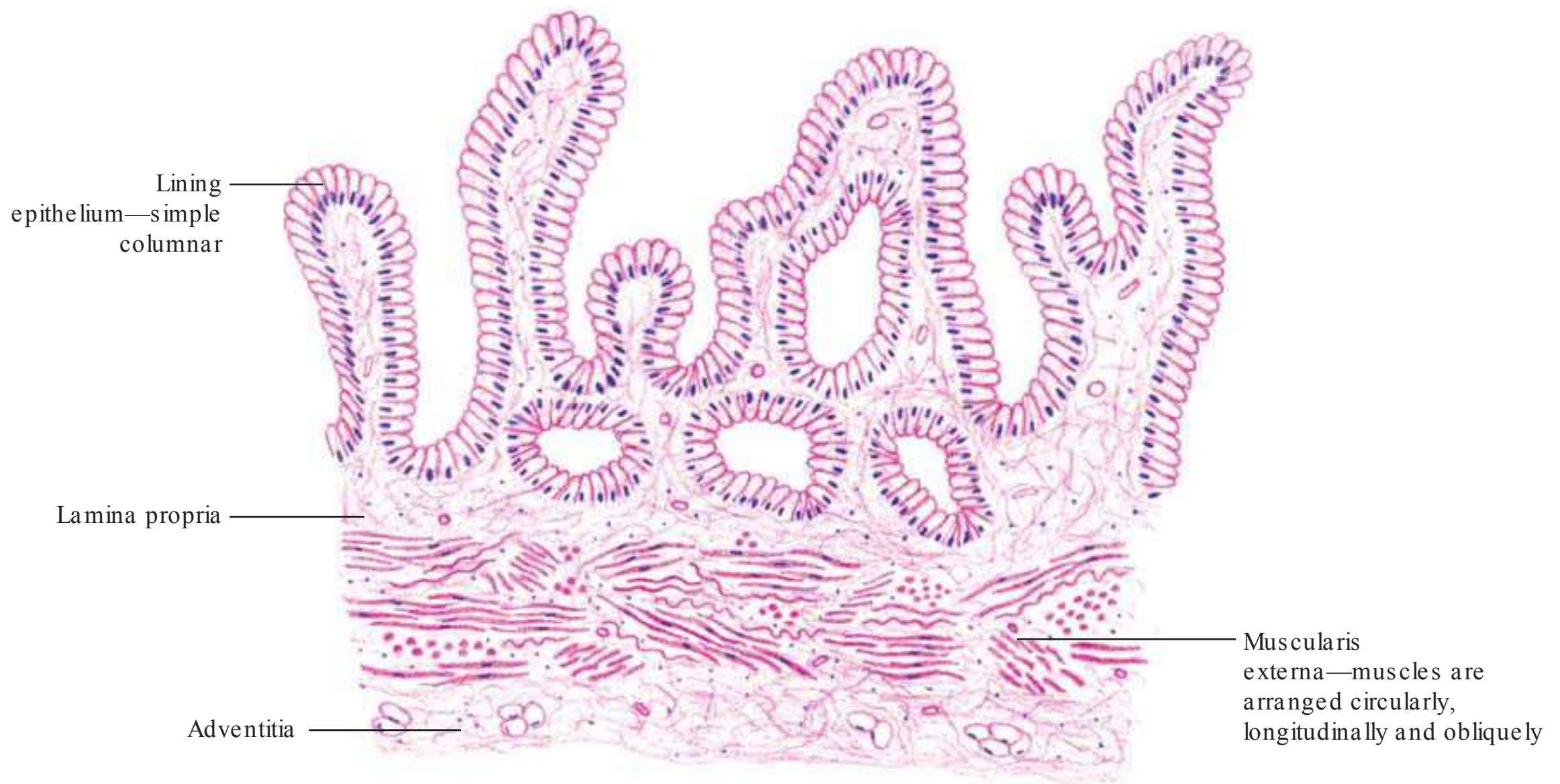
## **GALLBLADDER**

- The gallbladder is a blind sac, present at the inferior surface of the liver (Fig. 14.5).
- The neck of the gallbladder is continuous with the cystic duct, which joins the common hepatic duct to form the common bile duct. The common bile duct opens into the second part of the duodenum (Fig. 14.13).
- The gallbladder stores and concentrates bile.

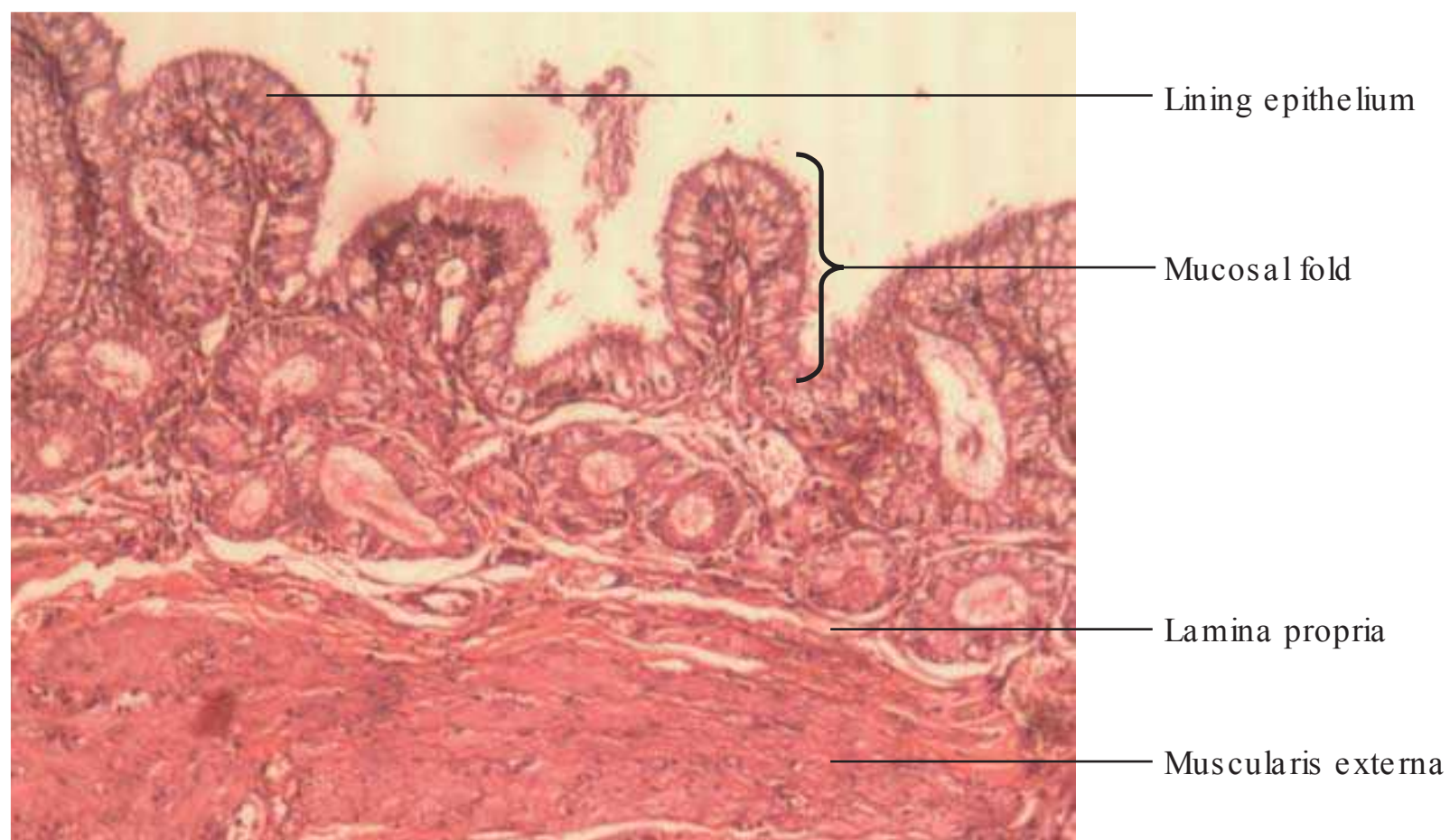
### **MICROSCOPIC FEATURES**

- Microscopically, the wall of the gallbladder consists of three layers (from lumen to outside):
  - (a) Mucosa
  - (b) Muscularis externa
  - (c) Adventitia and serosa (Fig. 14.16; PMG 14.8)
- There is no submucosa.





**Figure 14.16** Section of gallbladder (H&E pencil drawing).



**PMG 14.8** Gallbladder (H&E stain, X10).

## Mucosa

- In non-distended state, mucosa has numerous folds.
- Lining epithelium is simple columnar epithelium which lies over lamina propria; epithelial cells have microvilli.
- There is no muscularis mucosa.

## Muscularis Externa

- Bundles of smooth muscles are oriented in different planes (circularly, longitudinally and obliquely).
- In between the bundles of smooth muscles there are numerous collagen and elastic fibres.



- Contraction of these muscles (when stimulated by cholecystikin) causes expulsion of contents of the gallbladder into the cystic duct.

Adventitia and Serosa

- The part of the gallbladder covered with peritoneum has serosa and the part not covered with peritoneum has adventitia (like other retroperitoneal organs).
- On microscopic examination, mucosal folds of the gallbladder appear like the villi of small intestine. One of the important differentiating features is the presence of goblet cells in the mucosa of small intestine, which are absent in the gallbladder. Another differentiating feature is that in a particular region of small intestine, the size and shape of the villi are same, whereas in the gallbladder, the size and shape of the mucosal folds vary.

CLINICAL CORRELATES

Salivary Glands

- Benign tumours arising from the cells of ducts or myoepithelial cells are called pleomorphic adenoma. Warthin tumour is a benign tumour of parotid glands.

Liver

- Cirrhosis refers to irreversible chronic injury of the liver parenchyma, which results in disruption of the normal architecture of the entire liver. It is characterised by death of hepatocytes and scarring. Attempted regeneration of remaining hepatocytes results in irregular nodules, distortion of vascular architecture. Most common cause of cirrhosis of liver is alcoholic liver disease.

Pancreas

- Pancreatitis is the inflammation of the pancreas. In acute pancreatitis there is collection of inflammatory infiltrate in the stroma. Release of pancreatic enzymes can cause proteolytic digestion, haemorrhage and necrosis. It can become life-threatening. Common causes are alcoholism, gallstones, trauma, etc. Chronic pancreatitis can lead to fibrosis of the parenchyma.

KEYPOINTS

Basic Structure of Salivary Glands

Stroma	Parenchyma (Fig. 14.1)	Duct system (Fig. 14.1)
<ul style="list-style-type: none"><li>• Connective tissue capsule and its septa</li></ul>	<ul style="list-style-type: none"><li>• Serous acini: Cells are triangular in shape with round nuclei at their bases; apical cytoplasm is eosinophilic and basal cytoplasm is basophilic</li><li>• Mucous acini: Cells are tall with flat nuclei at their bases, empty-looking cells due to pale cytoplasm</li><li>• Serous demilunes: Serous cells arranged as a 'half moon' at one end of a mucous acinus</li></ul>	<ul style="list-style-type: none"><li>• Intercalated: Simple cuboidal epithelium</li><li>• Striated: Simple cuboidal epithelium; cells have basal striations</li><li>• Interlobular: Simple columnar epithelium in small ducts and stratified columnar epithelium in large ducts</li><li>• Terminal part: Stratified squamous non-keratinised epithelium</li></ul>

Different Types of Salivary Glands

Gland	Secretory acini	Differentiating features
Parotid (Fig. 14.2; PMG 14.1)	Serous	Darkly stained serous acini (note that pancreas also has similar appearance, but it has islets of Langerhans)

(continued)



(continued)

Gland	Secretory acini	Differentiating features
Sublingual (Fig. 14.3; PMG 14.2)	Mostly mucous, very few serous	Acinar cells appear empty, with fat nuclei at their bases
Submandibular (Fig. 14.4; PMG 14.3)	Mostly serous, few mucous; some mucous acini are capped with serous demilunes	Numerous serous acini; mucous acini with serous demilunes

Liver

Stroma	Parenchyma
<ul style="list-style-type: none"><li>Connective tissue covers the gland and enters the liver through hilum. It penetrates the parenchyma and carries blood vessels along with them.</li><li>Connective tissue divides the parenchyma into classical liver lobules.</li></ul>	<ul style="list-style-type: none"><li>In a liver lobule, hepatocytes are arranged in anastomosing plates around the central vein, separated by hepatic sinusoids.</li></ul>

Classical Lobule and Portal Lobule

Features	Classical lobule (Fig. 14.7; PMG 14.4 and 14.5)	Portal lobule (Fig. 14.10)
Basis of subdivisions	On structural basis: They are the structural units bounded by connective tissue	On the basis of the direction of flow of the bile
Shape of the lobule	Hexagonal	Triangular
Structure at the centre of the lobule	Central vein	Portal triad
Structure at the angles of the lobule	Portal triad: It contains three tubes—portal vein (the largest lumen), hepatic artery and bile duct	Central veins

Blood circulation: Portal vein and hepatic artery → hepatic sinusoids → central vein → sublobular vein → hepatic vein.

Pancreas (Fig. 14.14; PMG 14.6)

- Pancreas consists of the following :
  - (a) Exocrine part: It consists of pancreatic acini. The first portion of the duct system is lined by centroacinar cells. The duct system consists of intercalated, intralobular, interlobular and main pancreatic duct.
  - (b) Endocrine part: It is called islets of Langerhans and consists of polyhedral cells, arranged in irregular cords, separated by capillaries.
- The microscopic structure of pancreas resembles parotid glands; look for islets of Langerhans.

Gallbladder (Fig. 14.16)

- It consists of three layers: mucosa, muscularis externa and adventitia (serosa, in the part covered with peritoneum).
- Mucosal folds: The mucosal folds of the gallbladder can be confused with villi of the small intestine on microscopy.
  - (a) Goblet cells are present in mucosa of the small intestine but are absent in the gallbladder.
  - (b) In a particular region of the small intestine, the size and shape of the villi are same, whereas in the gallbladder, the size and shape of mucosal folds vary.

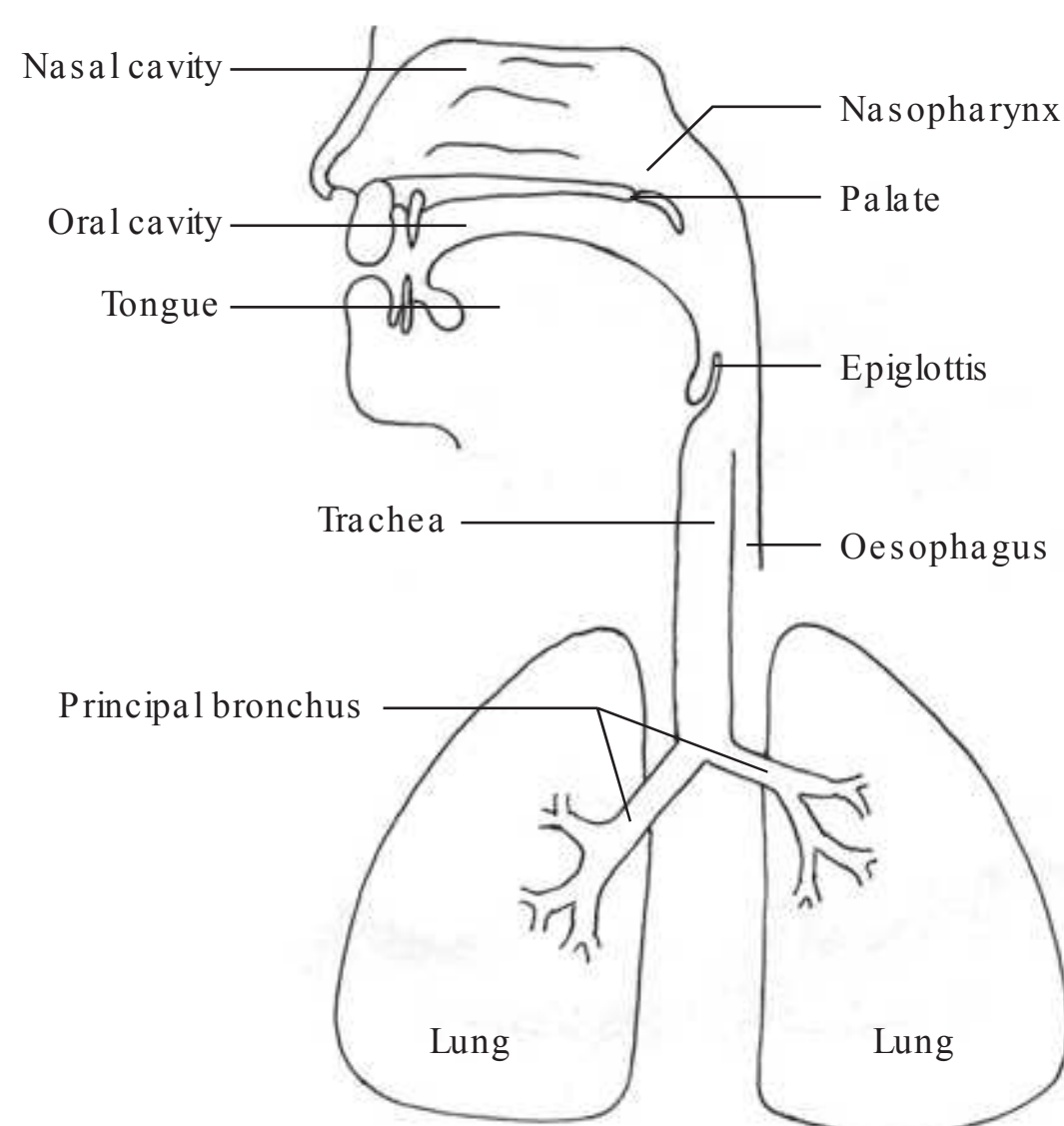
**SELF-ASSESSMENT**

1. Describe the different types of acini present in the salivary glands.
2. Describe the duct system of the salivary glands.
3. Describe the structure of a hepatic lobule.
4. What are the three structures in the portal triad? Which tube has the largest lumen?
5. What are Kupfer cells?
6. Compare the microscopic features of the pancreas with the parotid gland.
7. What are the layers of the wall of the gallbladder?



# Respiratory System

- The structures which are responsible for the inhalation of air, exchange of gases between the air and blood and exhalation of carbon dioxide constitute the respiratory system.
- Apart from respiration, this system is also responsible for olfaction and sound production.
- The respiratory system consists of two parts—a conducting part (which carries air) and a respiratory part (where gas exchange takes place).
- The conducting part consists of nasal cavity, paranasal sinuses, nasopharynx, larynx, trachea, bronchi, bronchioles and terminal bronchioles (Fig. 15.1).
- The respiratory part consists of respiratory bronchioles, alveolar ducts, alveolar sacs and alveoli.



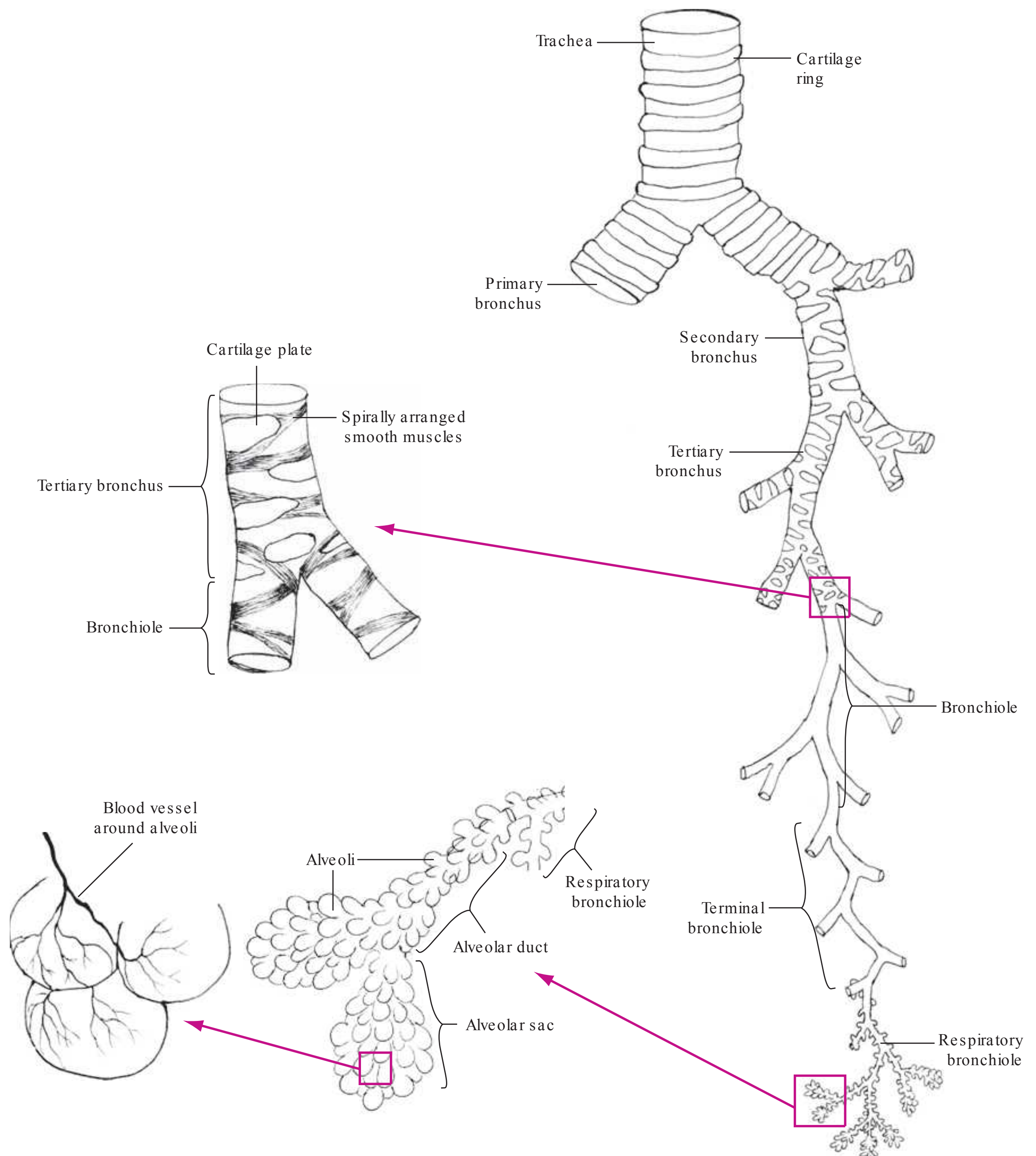
**Figure 15.1** Conducting part of the respiratory system.

## RESPIRATORY TRACT

- The respiratory tract begins from the nasal cavity. From the nasal cavity air enters the nasopharynx, the larynx and then into the trachea. From the trachea, the air enters the bronchial tree.
- Paranasal sinuses open in each nasal cavity.

**BRONCHIAL TREE (Fig. 15.2)**

- The bronchial tree begins with the bifurcation of the trachea and undergoes extensive branching. As the bronchial tree divides, the size of lumen decreases and there is enormous increase in the surface area for the gaseous exchange.
- The trachea divides into two primary or principal bronchi (singular: bronchus), one for each lung.



**Figure 15.2** Schematic diagram of the respiratory tree.



- The primary bronchus enters the lung and divides into secondary or lobar bronchi, one for each lobe (three for the right lung and two for the left lung).
- Secondary bronchi divide into numerous tertiary or segmental bronchi, each aerating its own territory in a lobe of the lungs (Fig. 15.2).
- The tertiary bronchi divide into numerous bronchioles which further divide into smaller bronchioles. The smallest bronchioles in airways are called terminal bronchioles. The conducting part of the respiratory tract ends at the terminal bronchioles, and airways distal to this constitute the respiratory part (though it is called respiratory part, it also conducts air) (Fig. 15.2).
- The terminal bronchiole divides and gives rise to respiratory bronchioles. The wall of respiratory bronchiole shows outpouchings, the alveoli (singular: alveolus), in which gaseous exchange takes place, and hence it is called respiratory bronchiole.
- As the respiratory bronchiole divides, there is a gradual increase in the number of alveoli in the distal airways.
- Respiratory bronchioles open into the alveolar duct. In the wall of the alveolar duct, the number of alveoli increases so much that they lie adjacent to one another. The walls of alveolar ducts appear to be entirely of alveoli (Fig. 15.2).
- Alveolar ducts open into the alveolar sacs (Fig. 15.2), which are clusters of alveoli.

### **GENERAL FEATURES OF THE WALL**

The walls of different parts of the respiratory tract show different features. In general, the wall of the respiratory tract consists of the following (from lumen to outside):

- Epithelium
- Lamina propria
- Layer of smooth muscles
- Submucosa
- Cartilage
- Adventitia

(See Figs 15.6 and 15.7 for histological components of the respiratory tract.)

### **Respiratory Epithelium**

- It is ciliated pseudostratified columnar epithelium with goblet cells. There is a gradual decrease in the height of the epithelial cells in distal airways. The epithelium loses goblet cells and cilia as it approaches the terminal parts of the tract.
- Goblet cells secrete mucus on the surface of the epithelium, and this mucus traps the inhaled particles.
- The cilia of the epithelial cells beat towards the pharynx, and they propel the mucus present on the surface of the cell towards the pharynx. From the pharynx, mucus is coughed out or swallowed. The respiratory epithelium has some more types of cells. Short or basal cells are the stem cells which divide and differentiate into the other types of cells present in the respiratory epithelium. Neuroendocrine cells are small cells scattered among the other cells of the epithelium, and these cells secrete serotonin.

### **Lamina Propria**

It is present underneath the epithelium and consists of loose connective tissue. In some regions, it has lymphoid nodules and mucous glands too. Respiratory epithelium along with lamina propria is called respiratory mucosa.

### **Smooth Muscles**

- A layer of smooth muscle is present underneath the lamina propria. It is seen in the airway distal to the trachea, till the alveolar duct. Bundles of smooth muscles are spirally arranged.

- The function of these muscles is to regulate the diameter (and resistance) of the airways. Parasympathetic stimulation of these muscles constricts airway passages, thereby increasing the airway resistance. Sympathetic stimulation dilates airways and decreases airway resistance.

### Submucosa

It is a layer of connective tissue, and it has mucous and serous glands. The ducts of these glands open into the lumen of the airways. Gradually, the presence of these glands decreases in the distal airway; they are seen till tertiary bronchi.

### Cartilage

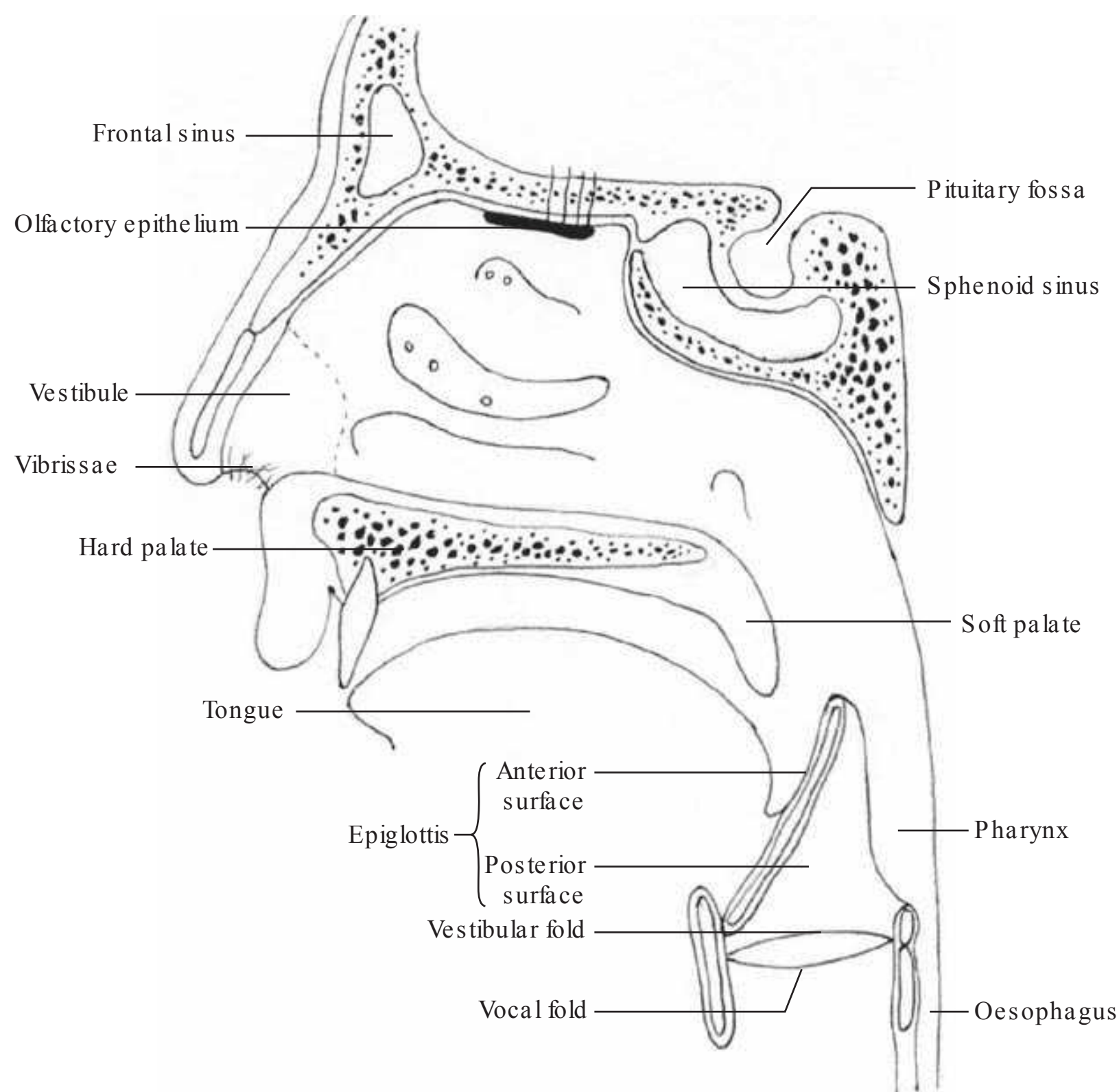
Underneath the submucosa, hyaline cartilage is present to support the wall of the airways. It prevents the airways from collapsing. It is present till tertiary bronchi.

### Adventitia

It is the outermost layer, which consists of connective tissue, and it blends with the surrounding tissues.

## NASAL CAVITY

- There are two nasal cavities separated by the nasal septum. Structurally and functionally, each cavity has three regions—vestibule, respiratory region and olfactory region (Fig. 15.3).
- The entrance of the nasal cavity is called vestibule. It is lined by skin (keratinised stratified squamous epithelium) having sebaceous and sweat glands and short thick hairs called vibrissae (Fig. 15.3).
- Behind the vestibule, there is the respiratory region of the nasal cavity; it is lined by the respiratory mucosa.



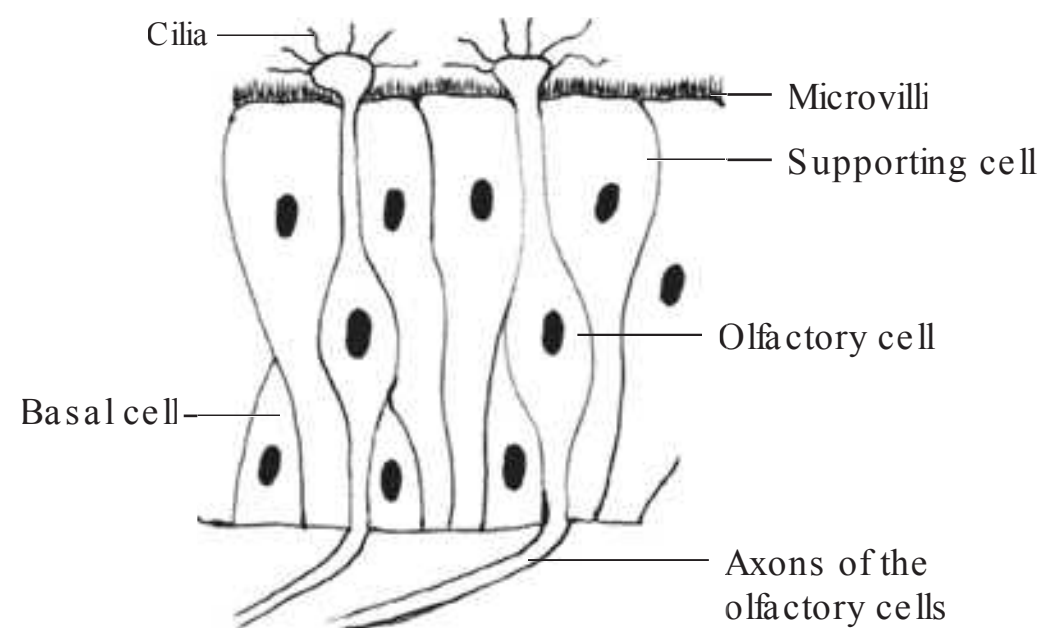
**Figure 15.3** Sagittal section of the nasal cavity, pharynx and larynx.



- The olfactory region is in the upper part of the nasal cavity; it is lined by olfactory epithelium which is pseudostratified columnar epithelium.
- The lamina propria of the nasal mucosa contains numerous seromucous glands; secretions of these glands add moisture to the inspired air.

### Olfactory Epithelium (Fig. 15.4)

- It is responsible for the sense of smell.
- It has three types of cells—supporting sustentacular cells, basal cells and olfactory cells.
- Supporting cells are tall with microvilli on their free surface.
- Basal cells are small, and they do not reach the surface.
- Olfactory cells are bipolar neurons. The apex of an olfactory cell expands to form the olfactory vesicle, and numerous non-motile cilia arise from it. The axons of the olfactory cells collect into bundles in the lamina propria.
- Lamina propria of olfactory epithelium has Bowman's glands. Watery secretions of these glands around the cilia provide a liquid medium into which olfactory substance dissolves.



**Figure. 15.4** Olfactory epithelium.

### PARANASAL SINUSES

- Paranasal sinuses are air-filled spaces in the bones around the nasal cavity.
- There are four pairs of paranasal sinuses—frontal, sphenoidal, ethmoidal and maxillary; they are present in the bones with the corresponding names.
- They open into the nasal cavity.
- They are lined by the respiratory mucosa.

### PHARYNX

- The pharynx is a muscular tube which serves as a common passage for the respiratory and gastrointestinal tracts.
- It lies behind the nasal and oral cavities and the larynx (Fig. 15.3). It consists of three parts—nasopharynx, oropharynx and laryngopharynx.
- The wall of the pharynx consists of three layers—inner (luminal) mucosa, middle muscular and outer adventitia.
- The lining epithelium of the nasopharynx is the respiratory epithelium. The walls of the oropharynx and laryngopharynx are subjected to mechanical injury during the swallowing of food; hence, these parts are lined by non-keratinised stratified squamous epithelium.

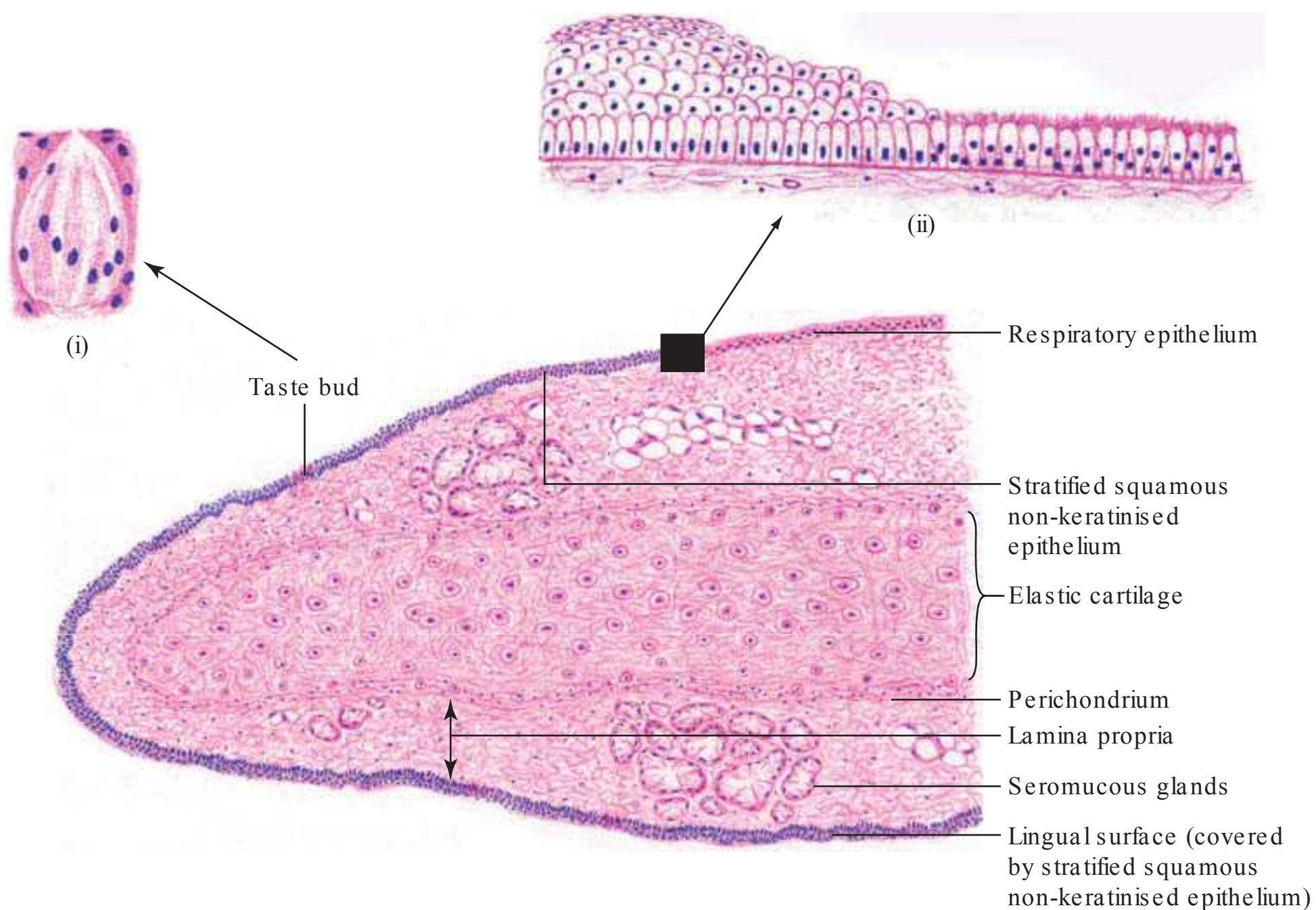
- Underneath the epithelium, there is the lamina propria which consists of connective tissue. In the lamina propria, numerous salivary glands are present; ducts of these glands open into the lumen of the pharynx. Numerous lymphoid tissues are also present in the lamina propria; these are mucosa-associated lymphoid tissue (MALT), discussed in detail in Chapter 11.

## LARYNX

- The larynx connects the oropharynx and the trachea. It is the component of the conductive part of the respiratory system, and it is also responsible for sound production.
- The interior of the larynx has two folds—vestibular and vocal folds—projecting into the lumen (Fig. 15.3).
- The vestibular fold (false vocal cord) is lined by respiratory epithelium. Underneath the epithelium, in the lamina propria, there are numerous serous and mucous glands; the ducts of these glands open into the luminal surface of the larynx.
- The vocal fold (true vocal cord) is lined by stratified squamous non-keratinised epithelium which provides protection from physical injury during its movement. The remaining parts of the interior of the larynx are lined by the respiratory mucosa.
- Underneath the lamina propria, laryngeal cartilages are present. These are thyroid, cricoid, epiglottis, corniculate and cuneiform cartilages; they are present in the wall of the larynx and form its skeletal framework. The thyroid, cricoid and most of arytenoid consist of hyaline cartilage whereas the epiglottis, corniculate and tips of the arytenoid are elastic cartilage.

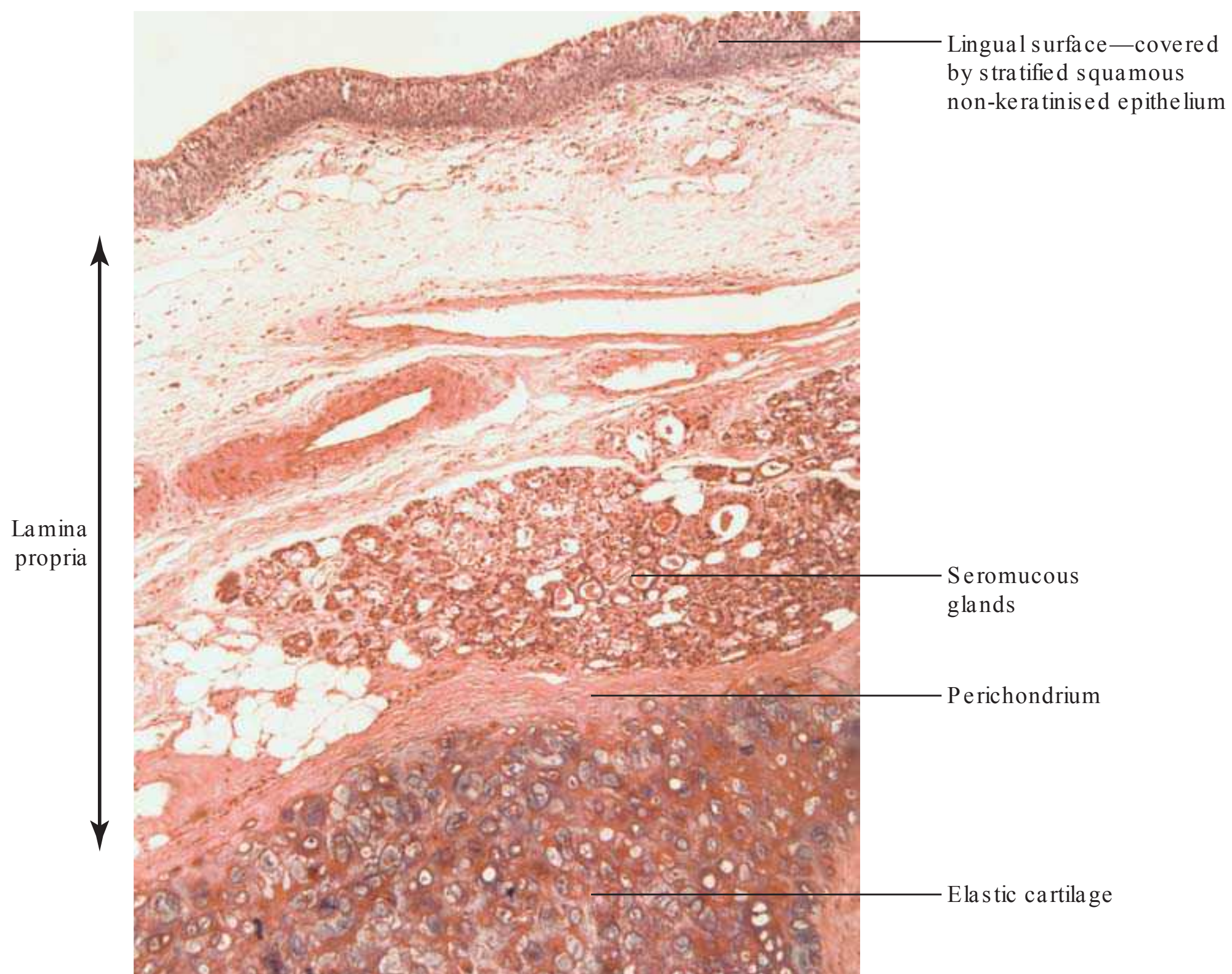
### Epiglottis (Fig. 15.5; PMG 15.1)

- The epiglottis has upper and lower ends, anterior and posterior surfaces and two lateral borders (Fig. 15.3).



**Figure 15.5** Section of epiglottis in low magnification. Inset (i) shows an enlarged view of taste bud. Inset (ii) shows junction of ciliated pseudostratified columnar epithelium (respiratory) and stratified squamous non-keratinised epithelium. (H&E pencil drawing)





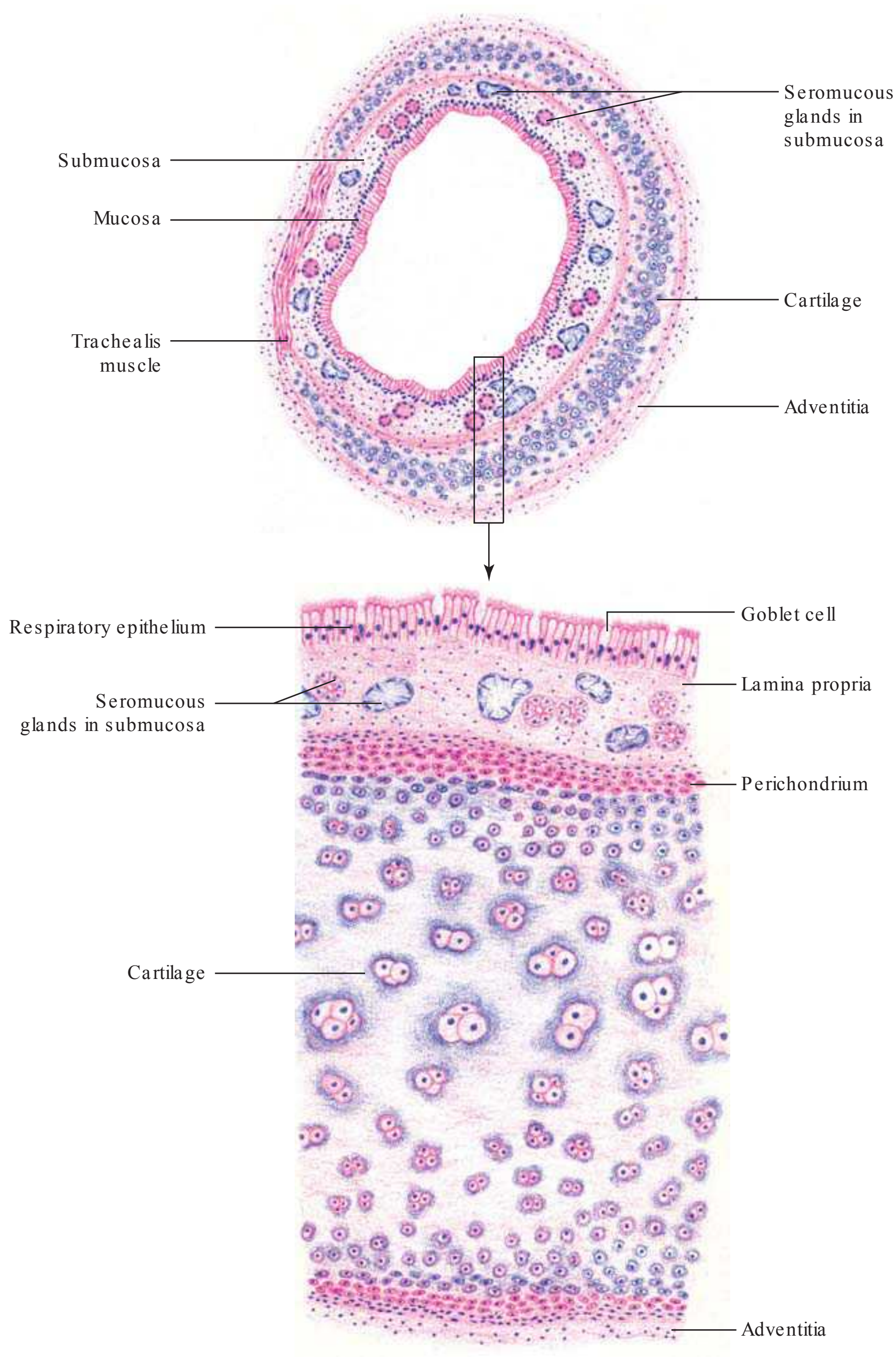
**PMG 15.1** Epiglottis (H&E stain, X5).

- The lingual surface (or anterior surface) and upper part of the laryngeal surface (or posterior surface) are covered by stratified squamous non-keratinised epithelium, and the rest of the laryngeal surface is covered by respiratory epithelium. The upper part of the laryngeal surface, where the epithelium is stratified squamous non-keratinised, shows the presence of some taste buds.
- Lamina propria consists of connective tissue with numerous serous and mucous glands.
- Elastic cartilage is present underneath the lamina propria and provides the skeletal framework to the epiglottis.

### **TRACHEA** (Fig. 15.6; PMG 15.2 and 15.3)

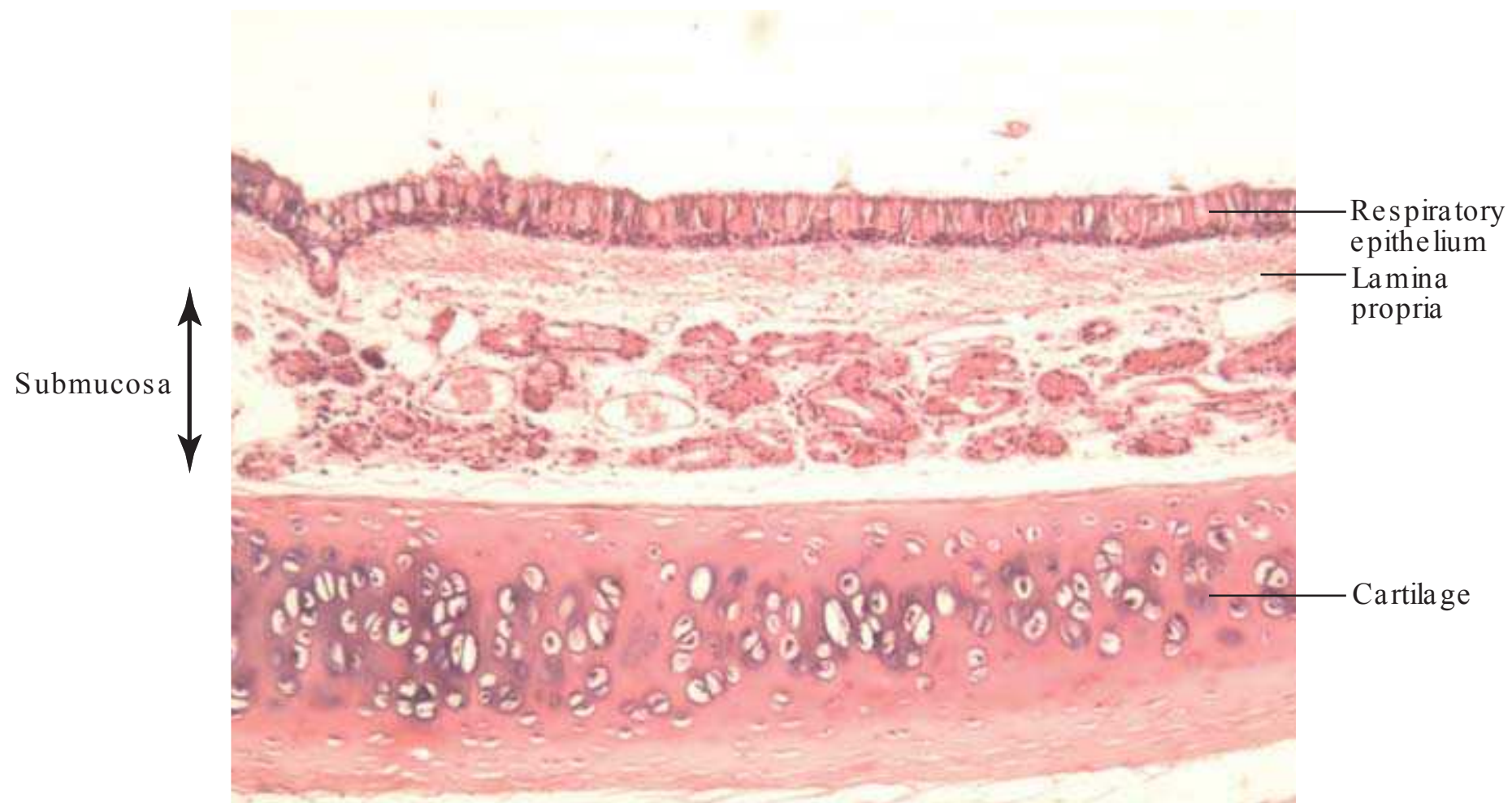
- The luminal surface of the trachea is lined by respiratory epithelium.
- Lamina propria is present underneath the epithelium.
- Underneath the lamina propria, there is the submucosa with serous and mucous glands; the ducts of these glands open on the luminal surface of the epithelium.
- Beneath the submucosa, there is 'C'-shaped hyaline cartilage. The ends of the 'C'-shaped cartilage are on the posterior aspect of the trachea. The two ends of these cartilages are joined by smooth muscle called trachealis (Fig. 15.6).



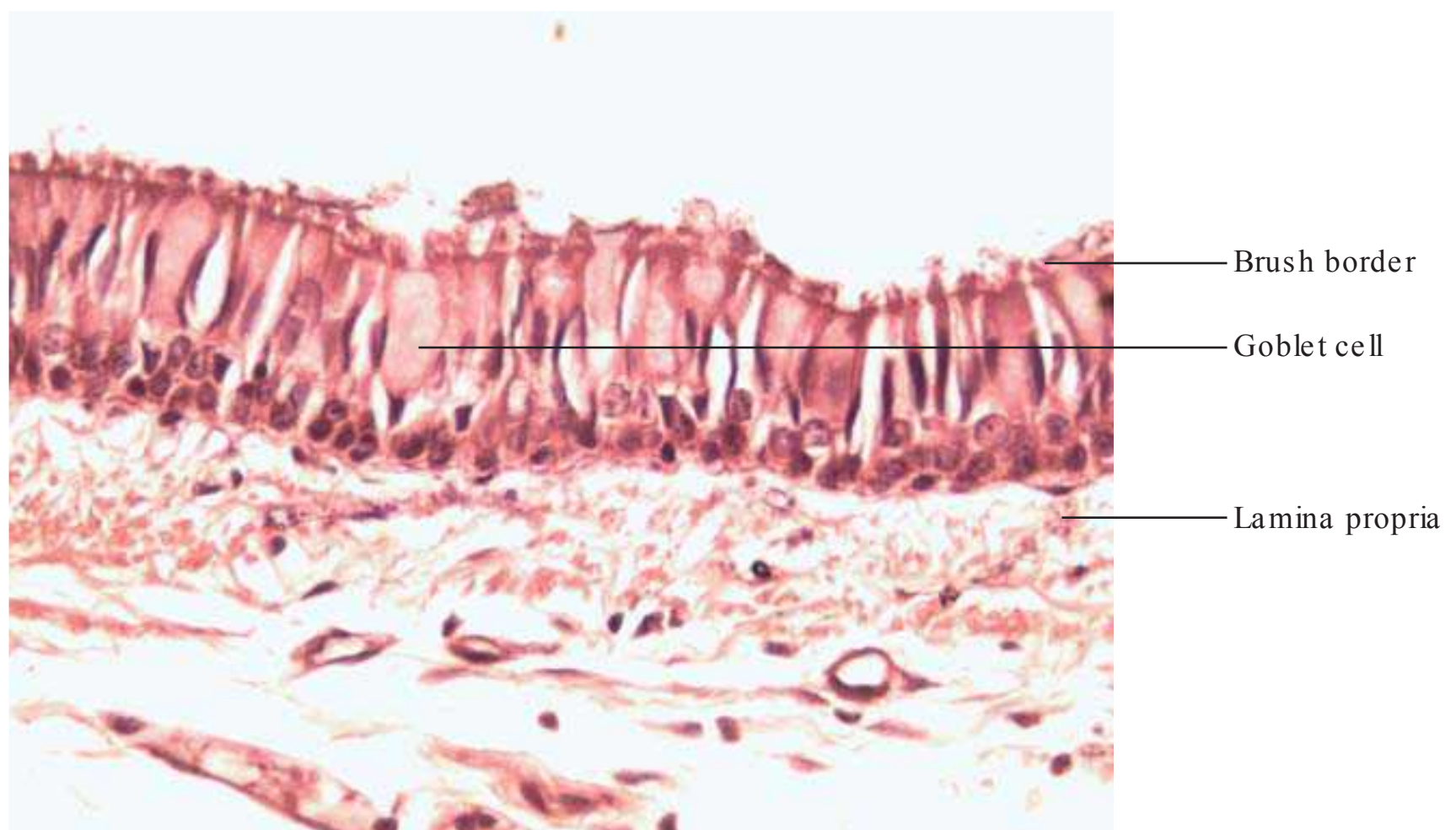


**Figure 15.6** Section of trachea in low magnification. Inset shows part of trachea in high magnification. (H&E pencil drawing)





**PMG 15.2** Trachea (H&E stain, X10).



**PMG 15.3** Respiratory epithelium of the trachea (H&E stain, X40).

## LUNGS

Like any other organ, lungs also consist of parenchyma and stroma. The airways inside the lungs constitute the parenchyma, whereas the connective tissue around the airways constitute the stroma of the lungs.

### **Primary or Principal Bronchus** (Fig. 15.2)

The primary bronchus is similar to the trachea with a few differences which are as follows:

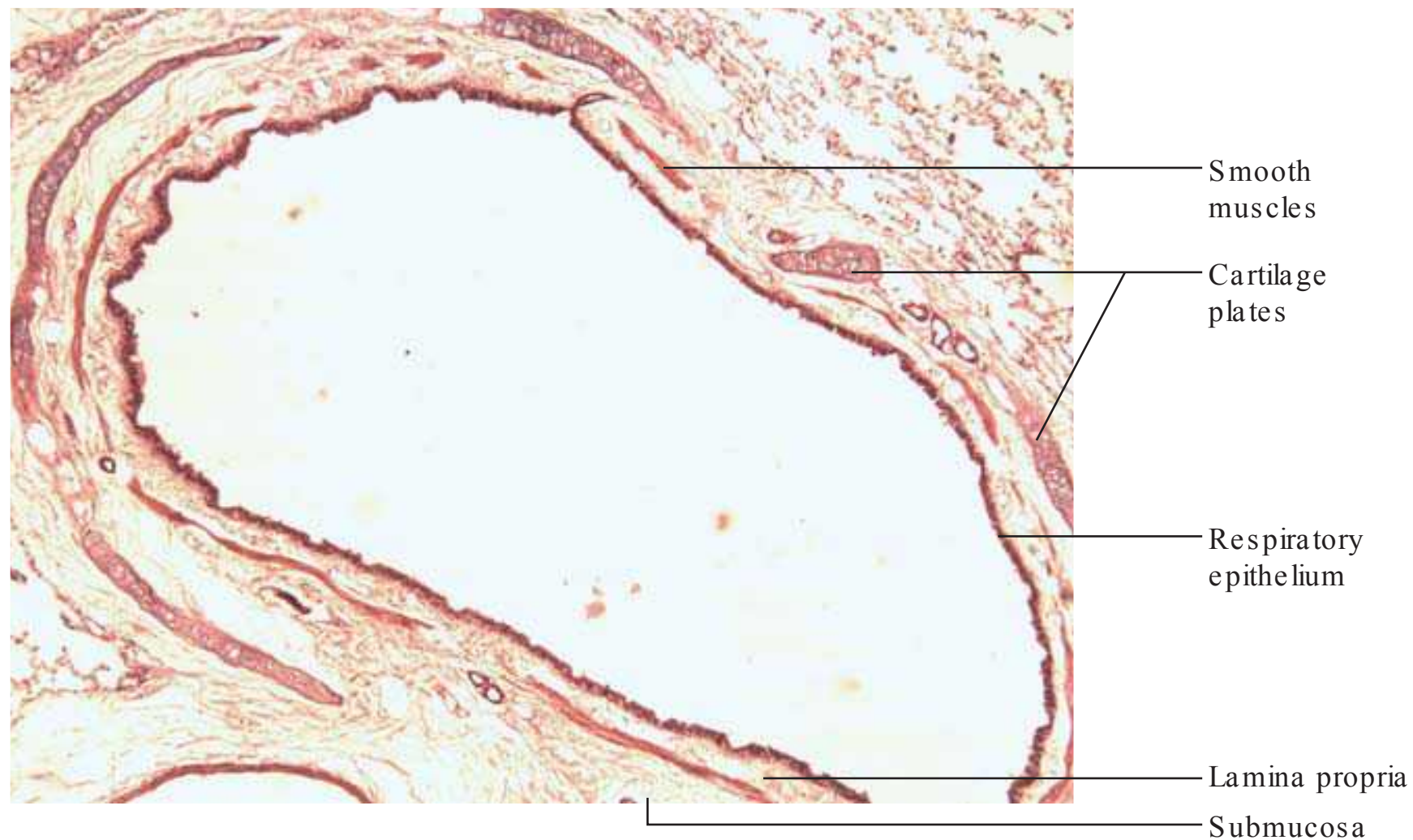
- The cells of respiratory epithelium are shorter and have less number of goblet cells.
- Between the lamina propria and the submucosa, there are bundles of spirally arranged smooth muscle, completely encircling the bronchus.
- Glands in submucosa are less in number compared to those in the submucosa of trachea.
- Cartilaginous rings completely encircle the bronchus.



**Secondary and Tertiary Bronchi** (Figs 15.2 and 15.7; PMG 15.4)

They are similar to the primary bronchus except for the following:

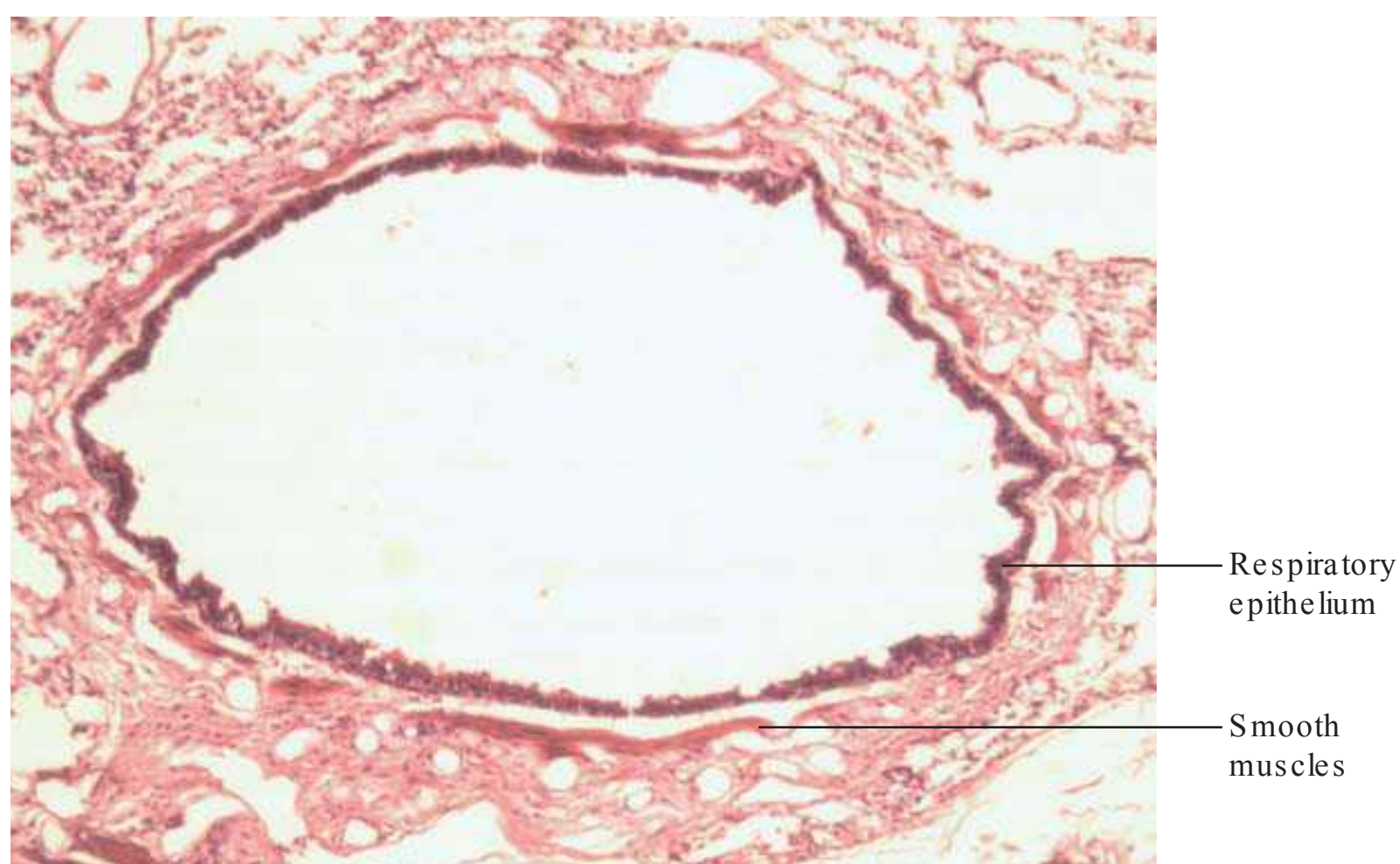
- The number of goblet cells is further reduced in the epithelium.
- The number of glands in the submucosa is also reduced.
- The cartilage is present as irregular plates.



**PMG 15.4** Intrapulmonary bronchus (H&Estain, X10).

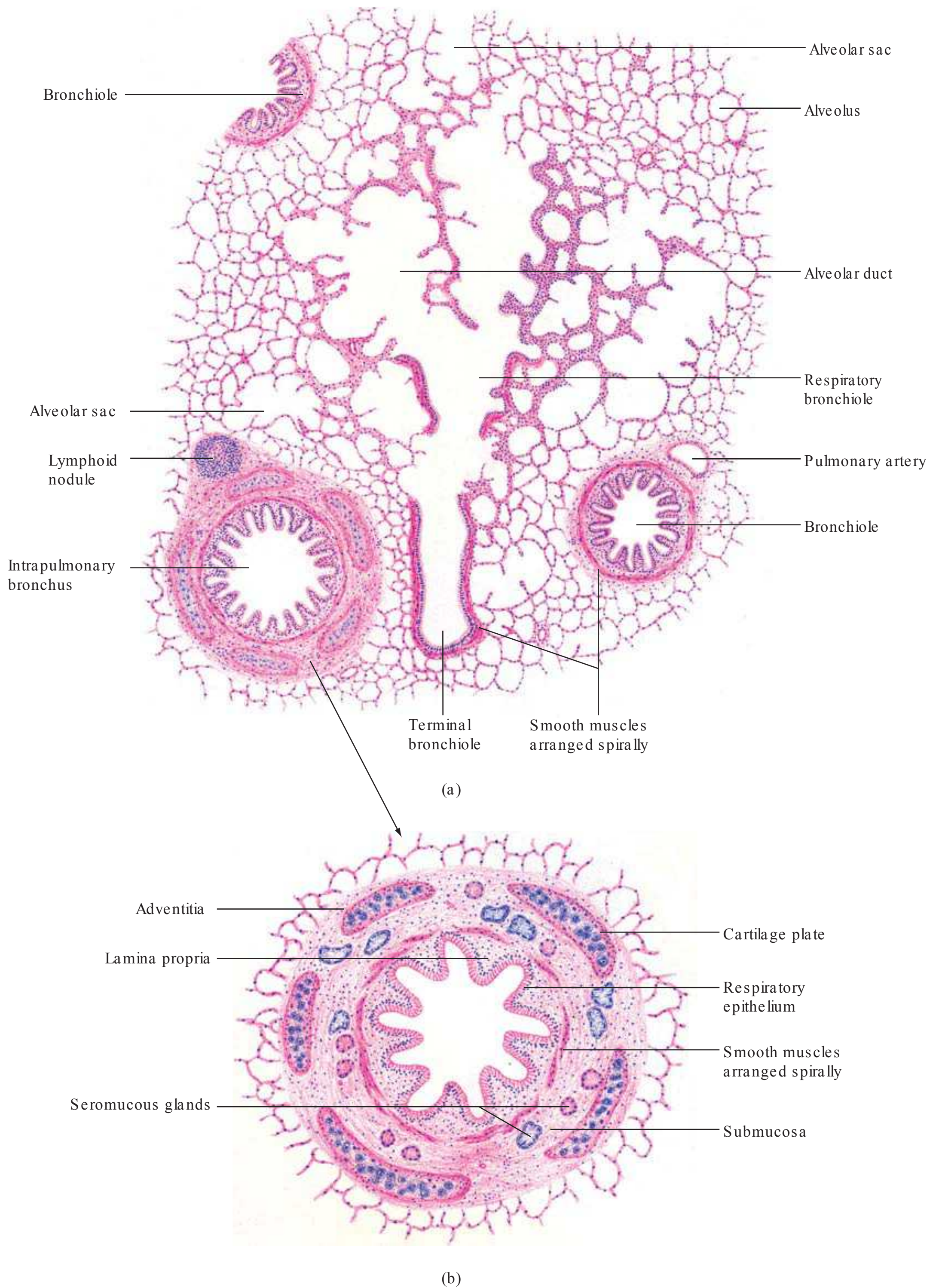
**Bronchiole** (Figs 15.2 and 15.7; PMG 15.5)

- The epithelium is ciliated, simple columnar or cuboidal.
- Terminal bronchiole is devoid of goblet cells.
- It has no glands.
- It has no cartilage.
- The smooth muscles are very prominent here.



**PMG 15.5** Bronchiole (H&Estain, X5).





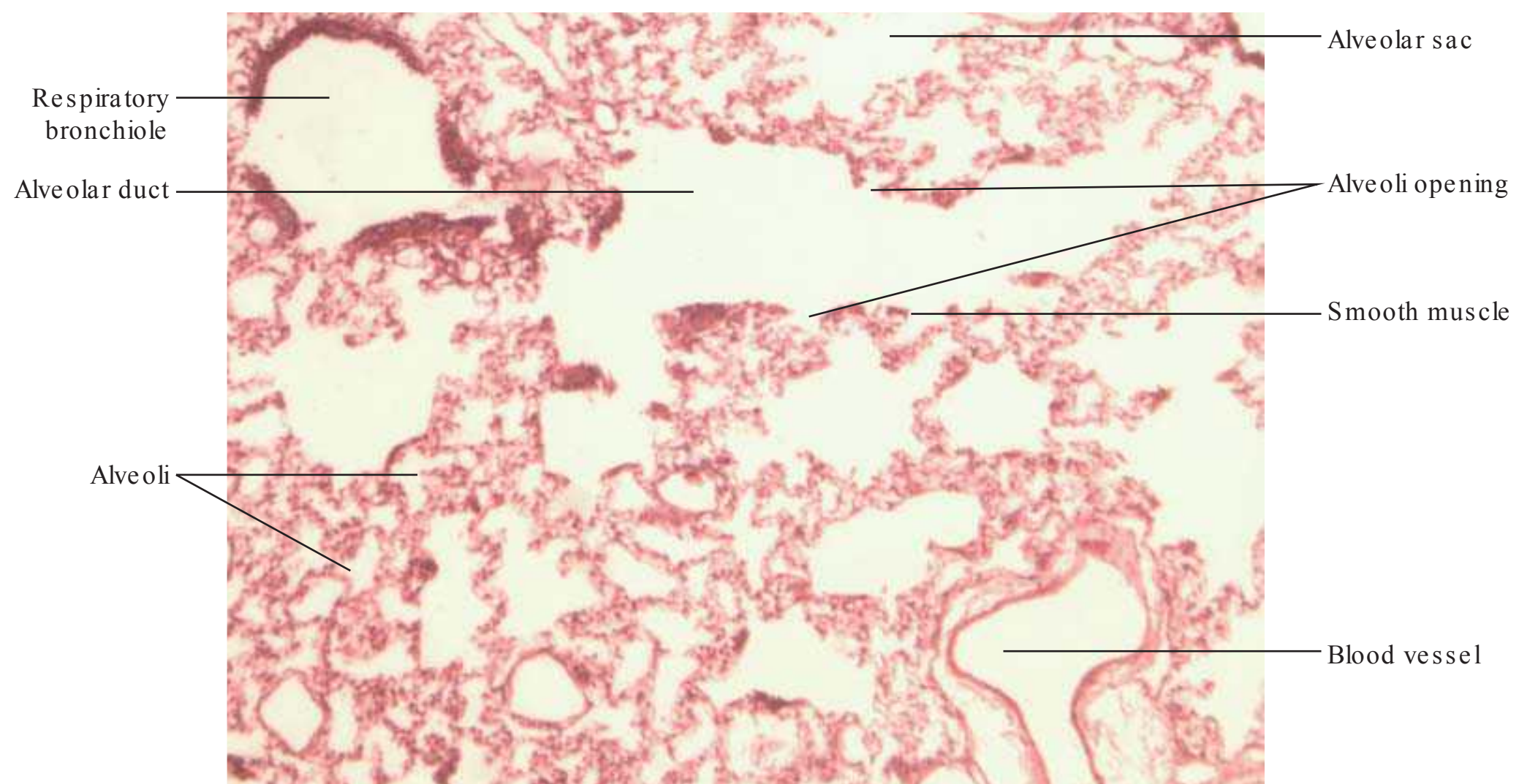
**Figure 15.7** Section of (a) lungs in low magnification and (b) intrapulmonary bronchi in medium magnification (H&E pencil drawing).



- In the epithelium of the terminal bronchiole, dome-shaped cells called Clara cells are also present, whose function is not known. They may provide some protection against inhaled toxins and carcinogens.

### *Respiratory Bronchiole* (Figs 15.2 and 15.7; PMG 15.6)

- The respiratory bronchiole is lined by simple cuboidal epithelium; these cells lack cilia.
- Goblet cells are absent.
- Epithelium is interrupted by alveoli, and at the opening of the alveoli the epithelium changes to simple squamous epithelium.
- The smooth muscle forms a ring around the opening of the alveoli.



**PMG 15.6** Section of lung showing respiratory bronchiole and alveolar duct (H&Estain, X10).

### *Alveolar Duct* (Figs 15.2 and 15.7; PMG 15.6)

- The wall of the alveolar duct consists of alveoli, lined by simple squamous epithelium.
- Underneath the epithelium, smooth muscles form rings at the opening of the alveolar sacs and alveoli, which are seen as a small bulge, in the wall in between two adjacent alveoli.
- Smooth muscles disappear in the terminal parts of alveolar ducts.

### *Alveolar Sac and Alveoli*

- The alveolar duct opens into dead end sacs, the alveolar sacs, which have openings of the alveoli (Figs 15.2 and 15.7; PMG 15.6).
- Alveoli increase the surface area for the gaseous exchange. Alveoli are surrounded by a network of capillaries (Fig. 15.2). The gaseous exchange occurs between the air present in the alveoli and the blood in the capillaries across their walls (see 'Interalveolar Septum').
- Alveoli are thin-walled outpouchings, lined by a single layer of cells; these cells are of two types: type I and type II cells, also called pneumocytes or alveolar cells. See Figure 15.8 for illustration of pneumocytes.



*Type I Pneumocytes*

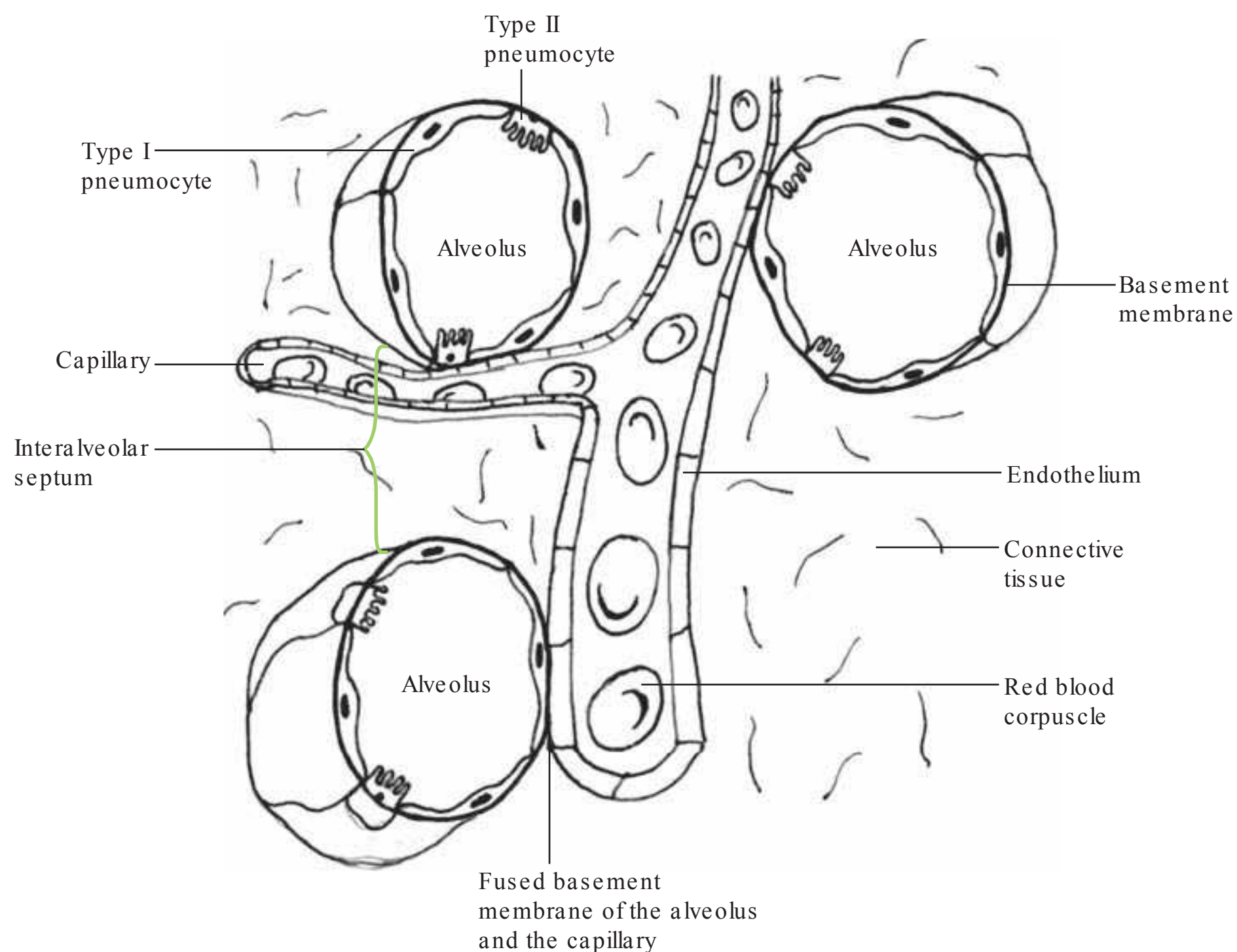
- These cells are squamous epithelial cells; adjacent cells are joined together by tight junctions.
- They cover most of the alveolar surface.
- These cells are involved in gaseous exchange.

*Type II Pneumocytes*

- These are cuboidal cells, scattered among type I cells.
- Compared to type I cells, their contribution to alveolar surface is very small. These cells are secretory cells. They secrete pulmonary surfactant, which lowers the surface tension and prevents alveoli from collapsing.
- Although the number of type I and type II cells is almost equal, type I cells form 90–95% of alveolar surface and type II cells contribute 5–10% of alveolar surface only. The small contribution to alveolar area by type II cells is due to their shape.

**Interalveolar Septum**

- It is the wall present in between the two adjacent alveoli (Fig. 15.8).
- It consists of epithelial cells of each alveolus on both sides, with connective tissue sandwiched between them. Capillaries are present in the connective tissue.
- Apart from the capillaries, the connective tissue in the interalveolar septum contains collagen and elastic fibres, fibroblasts and macrophages (dust cells).
- At some places, the capillary comes in contact with the alveolar surface. At these sites, the basement membrane of the capillary and the alveolus fuse (Fig. 15.8); this is the site of gaseous exchange.
- The interalveolar septa has numerous alveolar pores (pores of Kohn), which allow equalisation of pressure between the adjacent alveoli.



**Figure 15.8** Interalveolar septum.

*Air–Blood Barrier*

The oxygen molecule present in the alveolus diffuses across the epithelial cells lining the alveolus, the fused basement membrane of the alveolus and capillary, the endothelial cells of the capillary and finally into the red blood cell (Fig. 15.8).

**PULMONARY CIRCULATION**

- Lungs have dual blood supply through bronchial and pulmonary vessels.
- Bronchial vessels supply the conducting part of the lungs and pulmonary vessels supply the respiratory part.
- The blood vessels accompany the airways; they are present in the connective tissue that is present around the airways.
- At the level of the alveolar ducts, arterioles divide and form a capillary network around alveoli. These capillary networks are present in the interalveolar septum.

**LYMPHATIC CIRCULATION**

- Lymphatic vessels accompany the blood vessels.
- No lymphatic vessels are present in the alveolar sac and interalveolar septa.

**PLEURA**

- Pleura is a serous sac which covers the lungs.
- It consists of visceral and parietal layers. Between the two layers is a potential space known as pleural cavity which contains pleural fluid.
- The visceral layer lines the lungs and the parietal layer lines the interior of the thoracic cavity.
- Histologically, pleura consists of mesothelium (simple squamous epithelium) overlying a thin layer of vascular connective tissue.

**CLINICAL CORRELATES****Emphysema**

- It is characterised by abnormal permanent dilatation of airways distal to the terminal bronchiole. Dilatations occur due to destruction of the walls of the airways. Cigarette smoking and air pollution are the causative factors.

**Bronchiectasis**

- It is characterised by permanent dilatation of the bronchi and bronchioles due to damage to the muscles and elastic tissue.

**Bronchial Asthma**

- It occurs due to increased responsiveness of the airway to the allergen. The diameter of the airway is reduced due to contraction of the smooth muscles present in the airway.

**Pulmonary Oedema**

- It refers to accumulation of fluid within the lung parenchyma and air spaces of the lungs. The fluid entering the alveoli of the lungs prevents gaseous exchange. Pulmonary oedema is seen in left ventricular failure (it can occur in several other conditions also) when the left ventricle fails to empty completely. As a result backpressure develops in the left atrium, pulmonary veins and capillaries. Due to increase in capillary hydrostatic pressure, the fluid moves from the capillaries into the alveolar spaces.



# KEYPOINTS

## Epiglottis (Fig. 15.5; PMG 15.1)

- Lingual surface and upper part of laryngeal surface are covered by stratified squamous non-keratinised epithelium, and the rest of the laryngeal surface is covered by respiratory epithelium.
- Lamina propria has numerous serous and mucous glands.
- Elastic cartilage is present underneath the lamina propria.

## Trachea and Bronchial Tree

Part of the tract		Epithelium	Smooth muscle	Glands	Cartilage
Conducting part	Trachea (Fig. 15.6; PMG 15.2 and 15.3)	<ul style="list-style-type: none"> <li>Pseudostratified columnar epithelium with goblet cells</li> </ul>	Only on the posterior aspect, connecting the two ends of cartilage	Numerous serous and mucous glands in submucosa	'C'-shaped cartilage, deficient posteriorly
	Primary bronchus	<ul style="list-style-type: none"> <li>Cells are less taller</li> </ul>	Bundles of smooth muscles, present underneath the lamina propria; completely encircle the bronchus spirally	Less in number as compared to trachea	Cartilage completely encircles the bronchus
	Secondary and tertiary bronchi (Fig. 15.7; PMG 15.4)	<ul style="list-style-type: none"> <li>Less number of goblet cells</li> </ul>	Same as primary bronchus	Less number of glands	Cartilage plates are present
	Bronchiole (Fig. 15.7; PMG 15.5)	<ul style="list-style-type: none"> <li>Ciliated simple columnar or cuboidal epithelium</li> <li>A few goblet cells</li> </ul>	Very prominent	Absent	Absent
	Terminal bronchiole	<ul style="list-style-type: none"> <li>Clara cells</li> </ul>	Very prominent	Absent	Absent
Respiratory part	Respiratory bronchiole (Fig. 15.7; PMG 15.6)	<ul style="list-style-type: none"> <li>Simple cuboidal epithelium</li> <li>No cilia</li> <li>No goblet cells</li> <li>Alveoli lined by simple squamous cells</li> </ul>	Arranged as a ring at the opening of the alveoli	Absent	Absent
	Alveolar duct (Fig. 15.7; PMG 15.6)	<ul style="list-style-type: none"> <li>Wall has alveoli, lined by simple squamous epithelium</li> </ul>	Arranged as a ring at the opening of the alveolar duct and alveoli	Absent	Absent
	Alveolar sac and alveoli (Figs 15.7 and 15.8; PMG 15.6)	<ul style="list-style-type: none"> <li>Type I and type II pneumocytes</li> </ul>	Absent	Absent	Absent

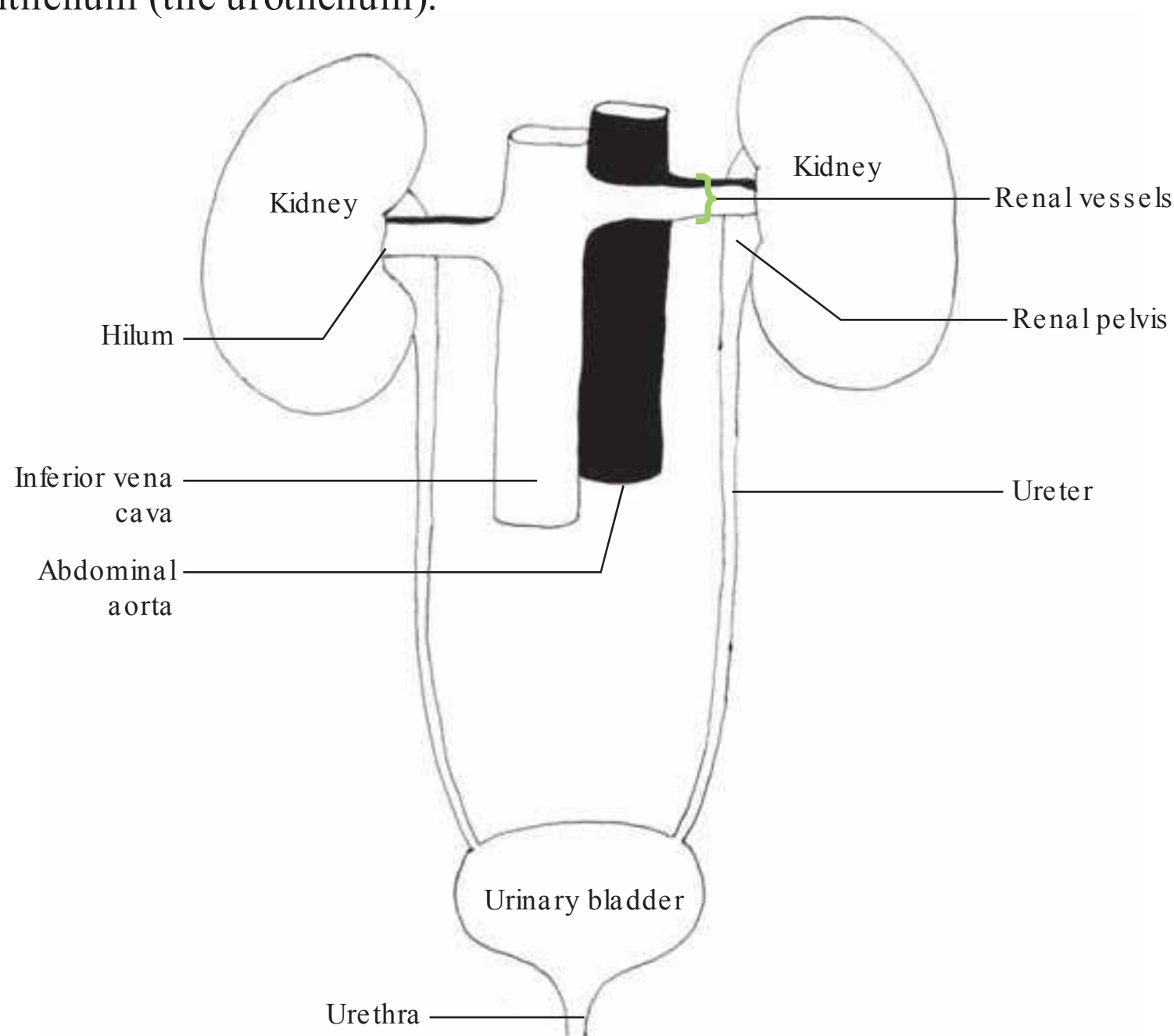
**SELF-ASSESSMENT**

1. Which parts of the airways constitute the conducting and respiratory parts of the respiratory tract?
2. Name the different layers of the wall of the trachea.
3. What changes are seen in the epithelium and the cartilage of the respiratory tract, from the trachea to the alveoli?
4. What are the differences in the microscopic structure of the bronchus and the bronchiole?
5. Name the types of cells lining the alveoli and list their functions.



# Urinary System

- The urinary system consists of a pair of kidneys and ureters, a urinary bladder and a urethra (Fig. 16.1).
- The main function of the urinary system is to remove metabolic waste from the blood, and this is achieved by urine production and excretion. Kidneys also help in regulating fluid and electrolyte balance and produce renin and erythropoietin.
- The urine produced by kidneys is conveyed outside the body by excretory passages. These passages consist of the minor and major calyces, renal pelvis, ureter, urinary bladder and urethra. These are hollow tubes. Except in urethra, the walls of these tubes have similar organisation and consist of mucosa, muscular layer and adventitia. Most of the excretory passage (except some parts of urethra) is lined by transitional epithelium (the urothelium).



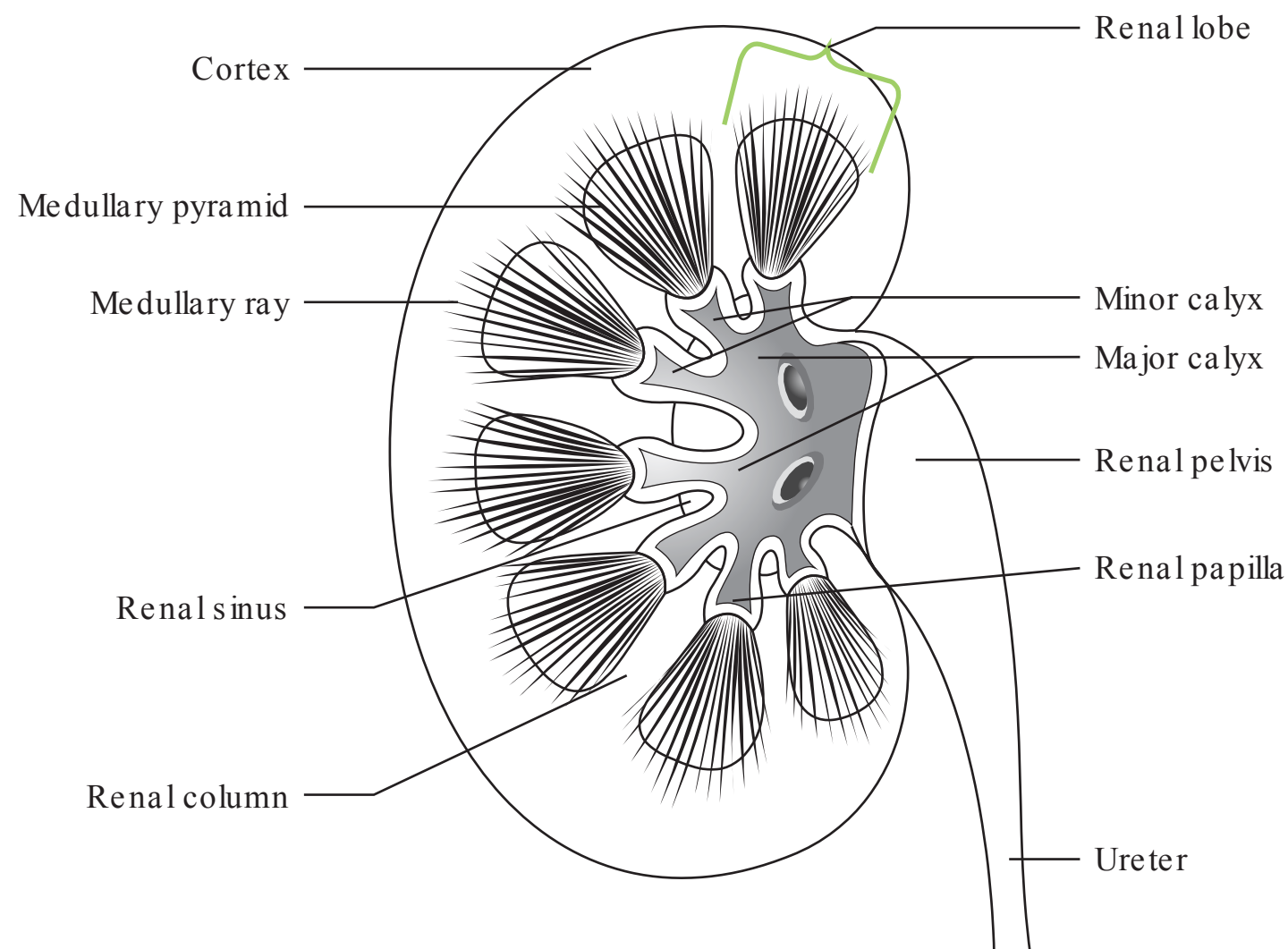
**Figure 16.1** Parts of the urinary system.

## KIDNEYS

- Kidneys are retroperitoneal organs located in the posterior abdominal wall.
- Each kidney is bean shaped and the medial border has central concavity known as hilum (Fig. 16.1). Through the hilum, the renal artery enters and the renal vein and the ureter leave the kidney.

## STRUCTURAL ORGANISATION

- A longitudinal section of the kidney shows that it consists of a capsule which covers the surface of the kidney. Underneath the capsule are the outer cortex and the inner medulla. The medulla surrounds the renal sinus (Fig. 16.2).



**Figure 16.2** Structural organisation of the kidney (sagittal section).

- Capsule is a layer of dense connective tissue that covers the kidney. It passes through the hilum and lines the renal sinus. Inside the renal sinus, it is continuous with the connective tissue of the walls of the calyces.
- Medulla: Each kidney consists of 10–15 medullary pyramids. The base of each pyramid is directed towards the cortex (Fig. 16.2), and the apex projects into the renal sinus. The apex of the medullary pyramid is known as renal papilla (Fig. 16.2; also see Fig. 16.9). The medullary pyramid contains the collecting ducts, loop of Henle, and vasa recta. Through the renal papilla, numerous collecting ducts pass, which are received by the funnel-shaped minor calyx (Fig. 16.2).
- Cortex is present underneath the capsule surrounding the medulla (Fig. 16.2). It contains the renal corpuscles, proximal and distal convoluted tubules, medullary rays and interlobular artery and veins. There are thin projections of medulla from the bases of medullary pyramids into the cortex, known as medullary rays (Fig. 16.2). It has the collecting tubules and ducts, and the straight portion of nephrons.
- Renal sinus is a cavity inside the kidney. It is surrounded by medullary pyramids and it communicates outside through the hilum (Fig. 16.2). It contains renal blood vessels, lymphatics, fat and minor calyces. The minor calyces join to form the major calyx which empties into a single funnel-shaped renal pelvis which in turn drains into the ureter.
- Renal lobes: One pyramid and part of the cortex overlying it together form one renal lobe (Fig. 16.2).
- Renal lobule: A medullary ray with its surrounding cortex constitutes a renal lobule. It is bounded on each side by interlobular vessels (described later under the section ‘Blood Supply of the Kidney’). In the centre of each renal lobule lies a medullary ray. All the nephrons of a renal lobule drain into the collecting ducts present in the medullary ray of the same lobule.

## MICROSCOPIC STRUCTURE

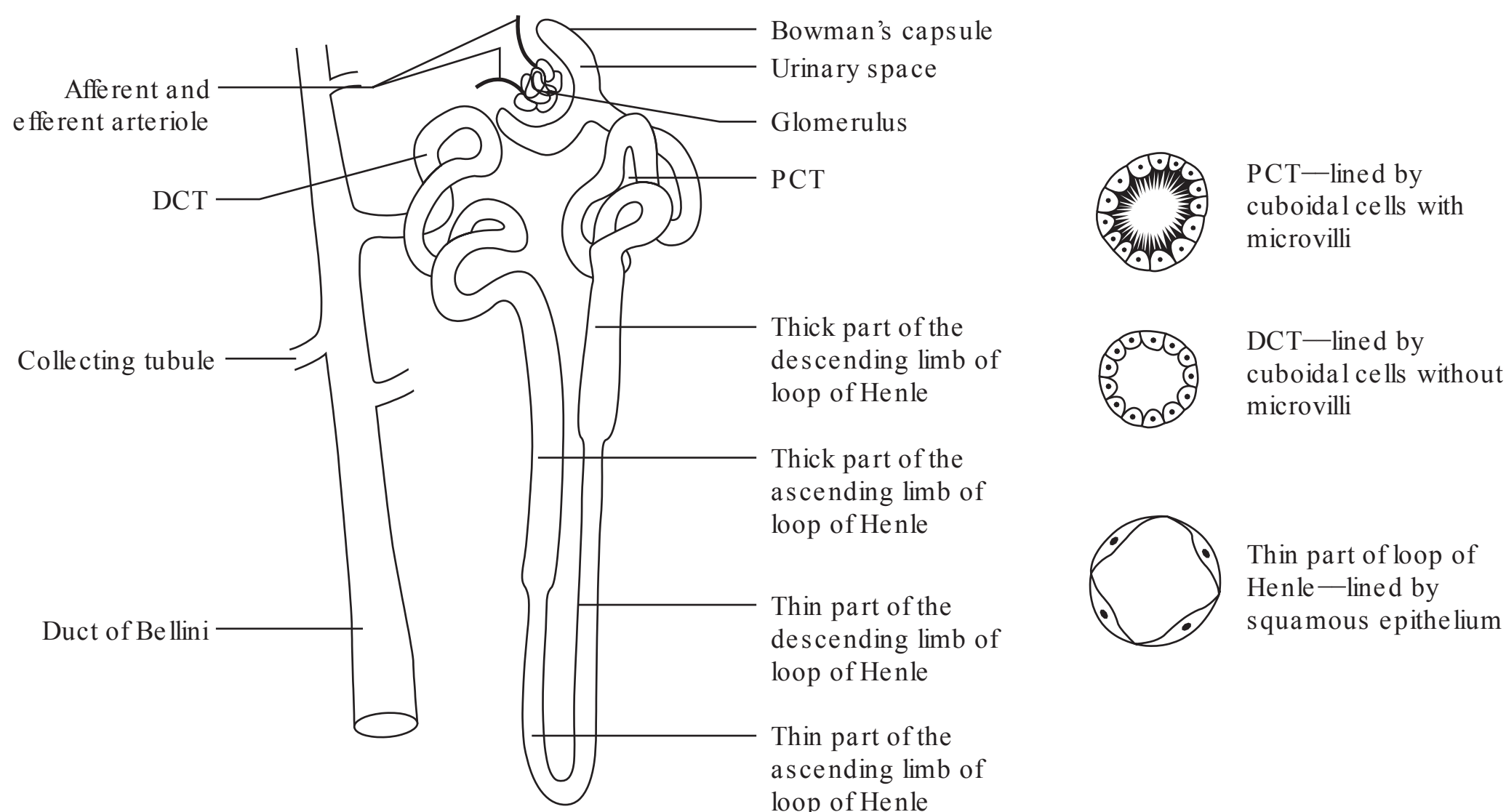
- Histologically, the kidney consists of three components: stroma, parenchyma and collecting system.
  - Stroma includes the capsule and the connective tissue which support the parenchyma, the interstitium.



- (b) Parenchyma consists of nephrons.
- (c) Collecting system includes the collecting tubules and ducts.

## Nephron

- Nephron is the structural and functional unit of the kidney.
- Major part of a nephron is located in the cortex and part of it is present in the medulla. It is illustrated in Figure 16.7.
- Each nephron consists of the following:
  - (a) Renal corpuscle: It consists of Bowman's capsule and glomerulus.
  - (b) Tubule: The tubule consists of a proximal convoluted tubule (PCT), a loop of Henle and a distal convoluted tubule (DCT) (Fig. 16.3).

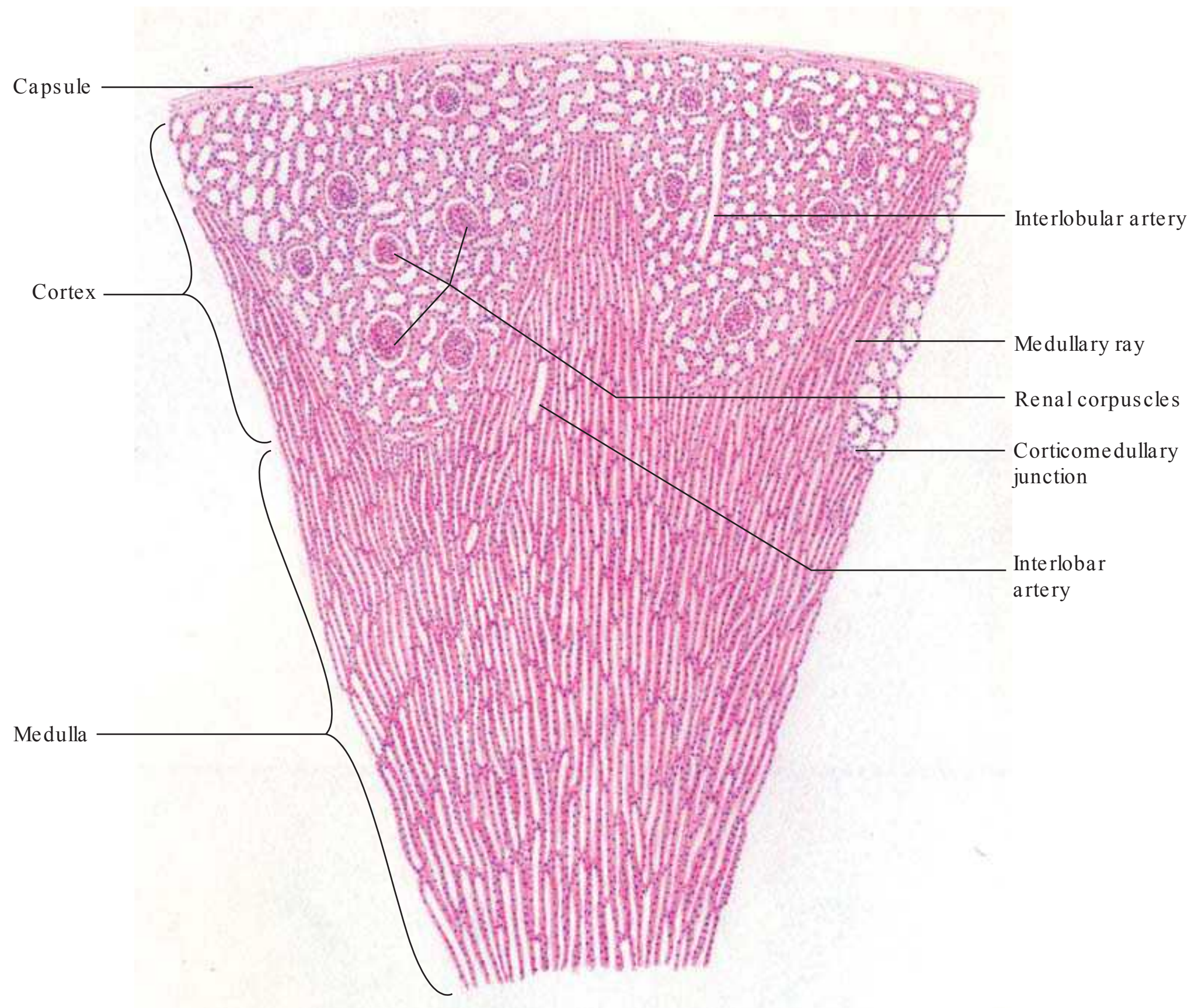


**Figure 16.3** Parts of nephron (on left) and transverse sections of PCT, DCT and loop of Henle (on right). DCT, distal convoluted tubule; PCT, proximal convoluted tubule.

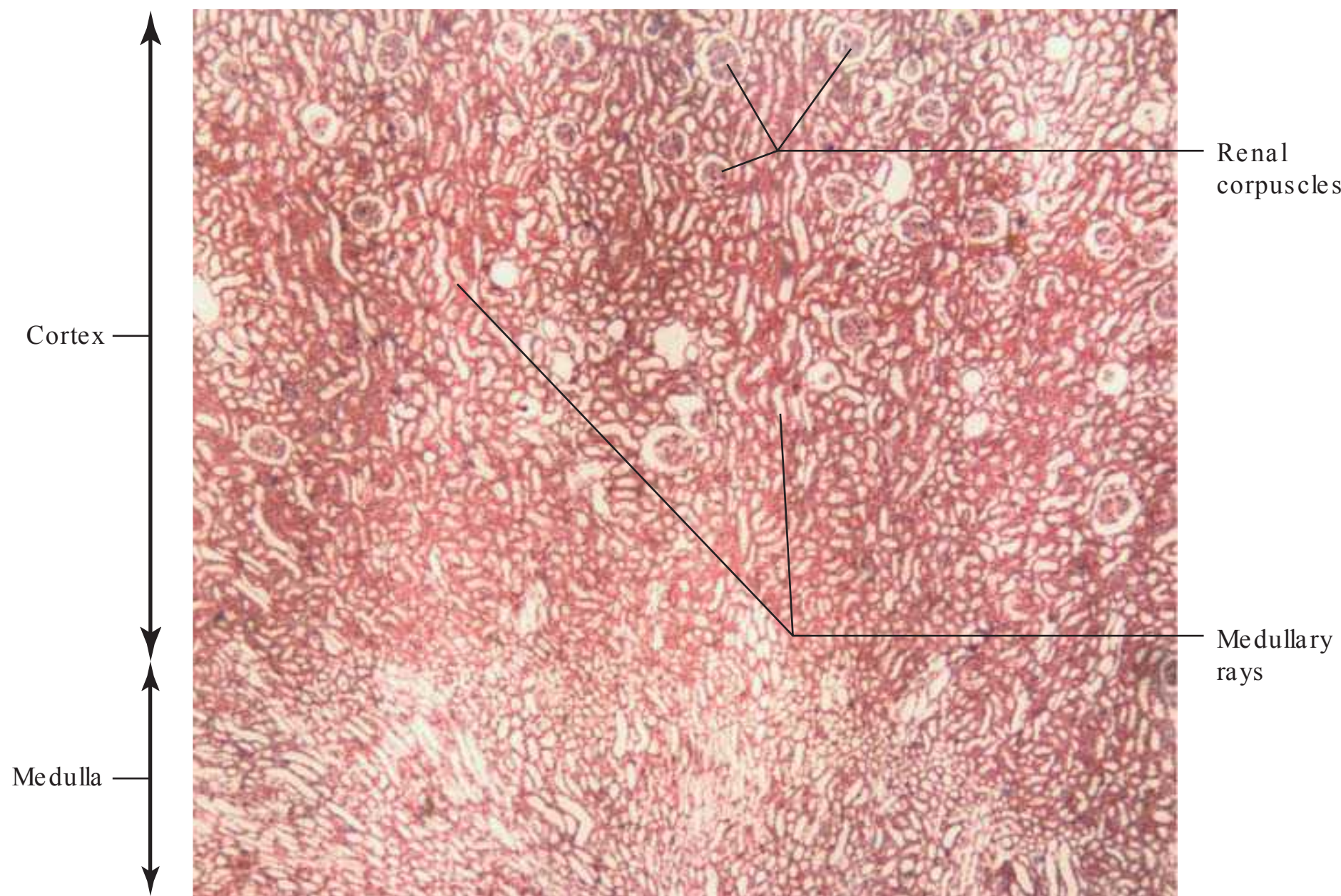
## Renal Corpuscle

- The part of nephron is present in the cortex (Figs 16.4 and 16.5; PMG 16.1).
- The part of the corpuscle where the afferent arteriole enters and the efferent arteriole leaves is called vascular pole, and the part of the corpuscle opposite to the vascular pole, where the PCT begins, is called urinary pole (Fig. 16.6).
- The renal corpuscle consists of Bowman's capsule and glomerulus (plural: glomeruli).
- Bowman's capsule is the blind beginning of the nephron. It is invaginated by a tuft of capillaries, the glomerulus. The afferent arteriole enters the renal corpuscle through the vascular pole and divides into capillaries (fenestrated); these capillaries join to form the efferent arteriole which leaves the glomerulus through the vascular pole.
- Bowman's capsule consists of two layers: parietal and visceral. The space between the two layers is called urinary or Bowman's space (Figs 16.3 and 16.6). Both layers of the Bowman's capsule are continuous with each other at the vascular pole of the renal corpuscle. The parietal layer consists of simple squamous epithelium resting on a basement membrane (Fig. 16.6) and the visceral layer consists of podocytes. Further details of podocytes are provided under 'Ultrastructure of Renal Corpuscle'.
- The process of urine formation begins with a filtrate of blood plasma at the renal corpuscles.



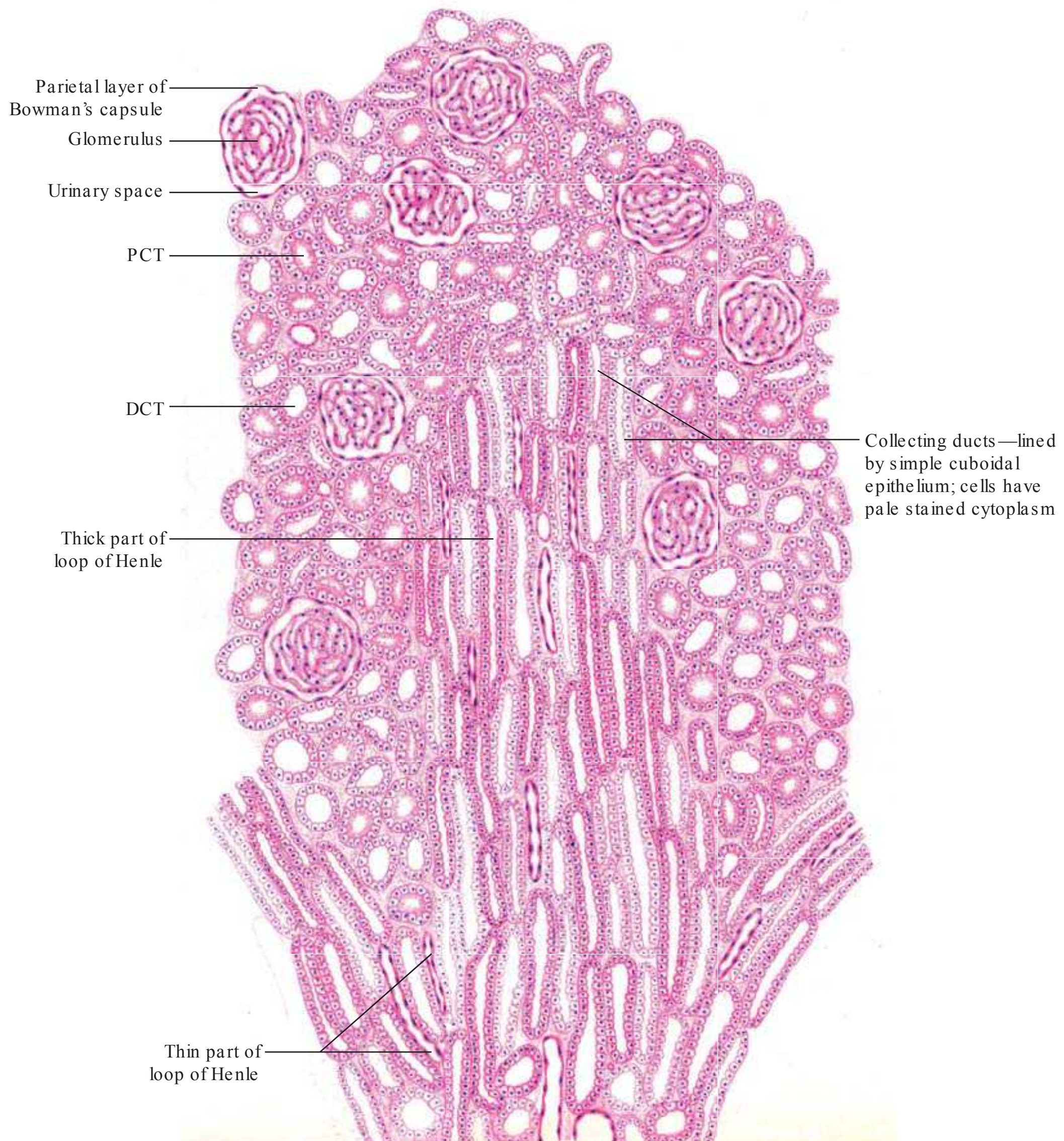


**Figure 16.4** Section of kidney in low magnification (H&E pencil drawing).



**PMG 16.1** Kidney (H&Estain, X2.5).





**Figure 16.5** Section of kidney in high magnification (H&E pencil drawing). DCT, distal convoluted tubule; PCT, proximal convoluted tubule.

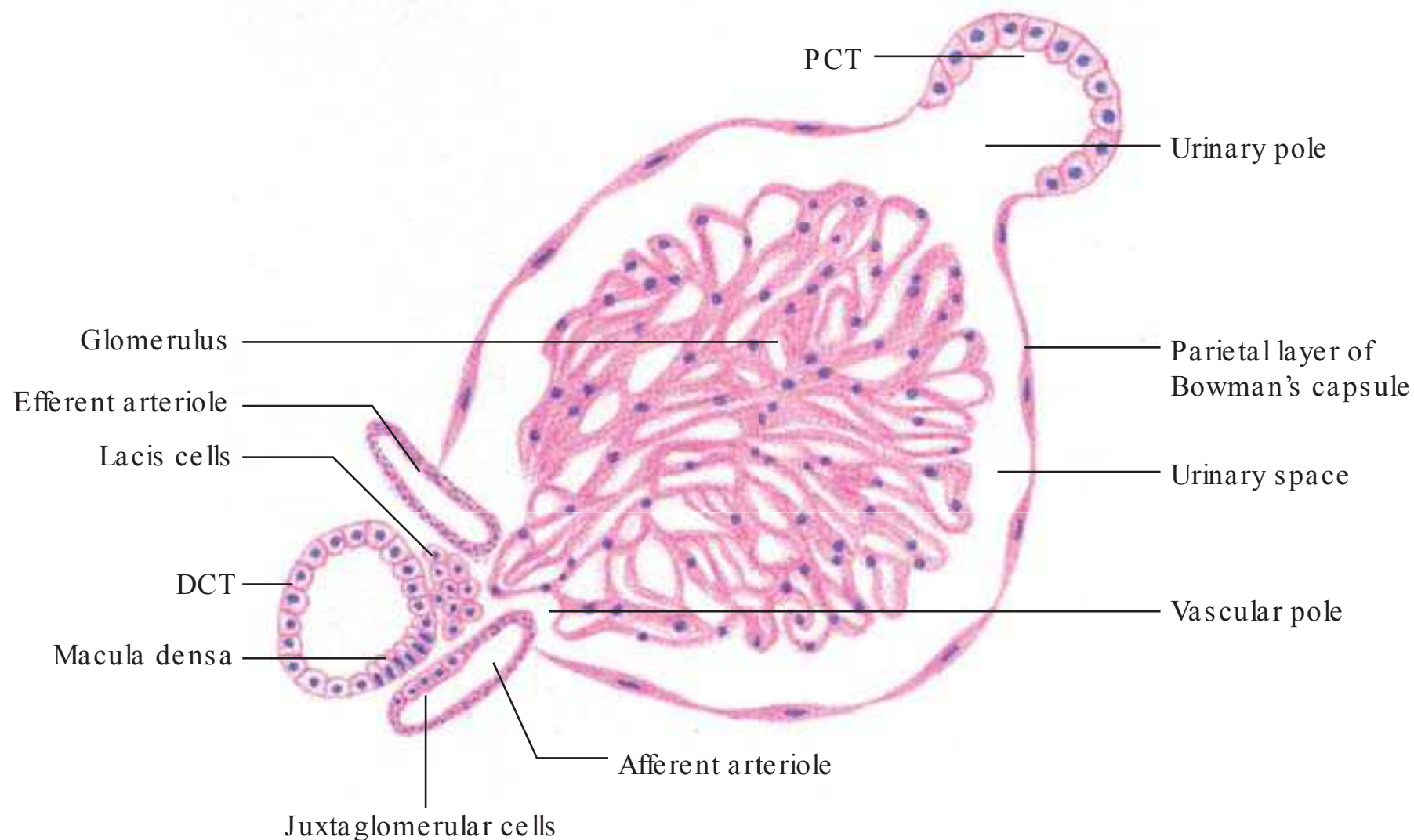
### *Tubule*

As mentioned earlier, the tubule of a nephron consists of a PCT, a loop of Henle and a DCT. The tubule consists of epithelial cells resting on a basement membrane. The basement membrane of the parietal layer of the Bowman's capsule is continuous with the basement membrane of the tubule. The epithelial cells lining a tubule vary in different parts of the tubule.

#### **1. Proximal convoluted tubule (PCT)**

- PCT is the longest part of the nephron and is present in the cortex.
- It begins at the urinary pole of the renal corpuscle.
- It is lined by simple cuboidal epithelium with microvilli (brush border). The microvilli increase the surface area for absorption (Fig. 16.5; also see Fig. 16.3).





**Figure 16.6** Magnified view of juxtaglomerular apparatus (H&E pencil drawing). DCT, distal convoluted tubule; PCT, proximal convoluted tubule.

- In PCT, reabsorption of various components of glomerular filtrate occurs. Sodium along with water, amino acids, glucose, chloride and bicarbonate are restored to the blood. About 75% of glomerular filtrate is reabsorbed.

## 2. Loop of Henle

- It is a 'U'-shaped tube arising from the PCT, which descends from the cortex into the medulla and then returns back into the cortex and ends into the DCT.
- It has descending and ascending limbs. The descending limb begins as a continuation of PCT and ends at the bend of the loop. The ascending limb begins at the bend of the loop and ends in DCT. Each limb has thin and thick parts. The parts of the loop of Henle from PCT to DCT are as follows: thick part of the descending limb, thin part of the descending limb, thin part of the ascending limb and thick part of the ascending limb. (Fig. 16.3).
- Thick parts are lined by cuboidal and thin part is lined by squamous epithelium (Fig. 16.5).
- The loop of Henle helps in increasing the osmotic gradient in the medulla. This gradient allows concentration of the urine in the collecting ducts as it passes through the medulla.

## 3. Distal convoluted tubule (DCT)

- It is present in the cortex.
- It is the continuation of the ascending limb of the loop of Henle as it returns to the cortex (Fig. 16.3).
- It is lined by simple cuboidal epithelium. Unlike the PCT, cells of the DCT do not have microvilli (Figs 16.3 and 16.5).
- In the DCT,  $\text{Na}^+$  is reabsorbed from the filtrate into the interstitium and  $\text{K}^+$  and  $\text{H}^+$  move from the interstitium into the filtrate, under the influence of aldosterone hormone.
- Macula densa: The cells of the wall of the DCT, coming in close contact with the afferent arteriole of the glomerulus, are closely packed columnar cells, which form macula densa (Fig. 16.6). These cells are sensitive to the concentration of sodium ions in the fluid of the DCT. Macula densa is one of the components of juxtaglomerular apparatus (described later).



## Collecting System

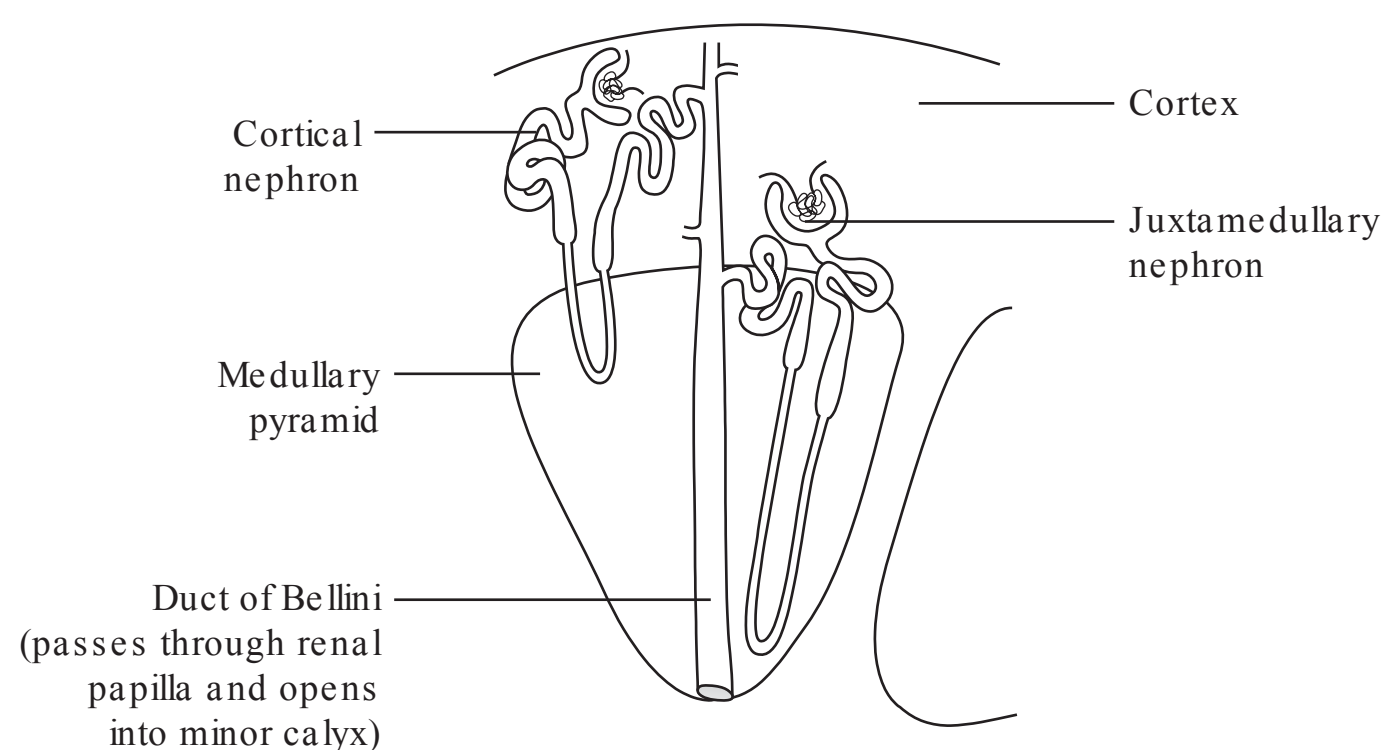
- The collecting system consists of the following:
  - (a) Collecting tubules (small ducts)
  - (b) Ducts
- The DCT empties into the collecting tubules, which pass through the medullary ray and join with other collecting tubules to form larger ducts (duct of Bellini) (Fig. 16.3).
- Larger ducts enter the medullary pyramid, pass through the renal papillae and open into the minor calyces.
- The collecting system is lined by simple epithelium which rests on a basement membrane. Tubules are lined by cuboidal cells and ducts are lined by columnar cells; these cells have pale-stained cytoplasm (Fig. 16.5).
- In the presence of antidiuretic hormone (ADH), the cells of the collecting tubules and ducts become permeable to water. Due to the hypertonic osmotic gradient in the interstitium of the medulla, the water moves out of the lumen of the tubules as they pass through the medulla and helps in formation of hypertonic urine.

## Interstitium

- Interstitium is the connective tissue present around the components of the renal parenchyma, that is it occupies the space between glomeruli, tubules, ducts, vessels and nerves.
- The volume occupied by the interstitium in the cortex is less (8–10%), but it increases significantly in the medulla (25–30% of the medullary volume).
- It consists of interstitial cells and matrix.
- The interstitial cells resemble fibroblasts.

## Types of Nephrons

- There are two types of nephrons: cortical and juxtamedullary (Fig. 16.7).
- Majority of the nephrons are cortical nephrons, and their renal corpuscles are present in the renal cortex.
- The renal corpuscles of the juxtamedullary nephrons are located in the cortex, close to the medulla. These nephrons have long loops of Henle extending deep into the medulla.



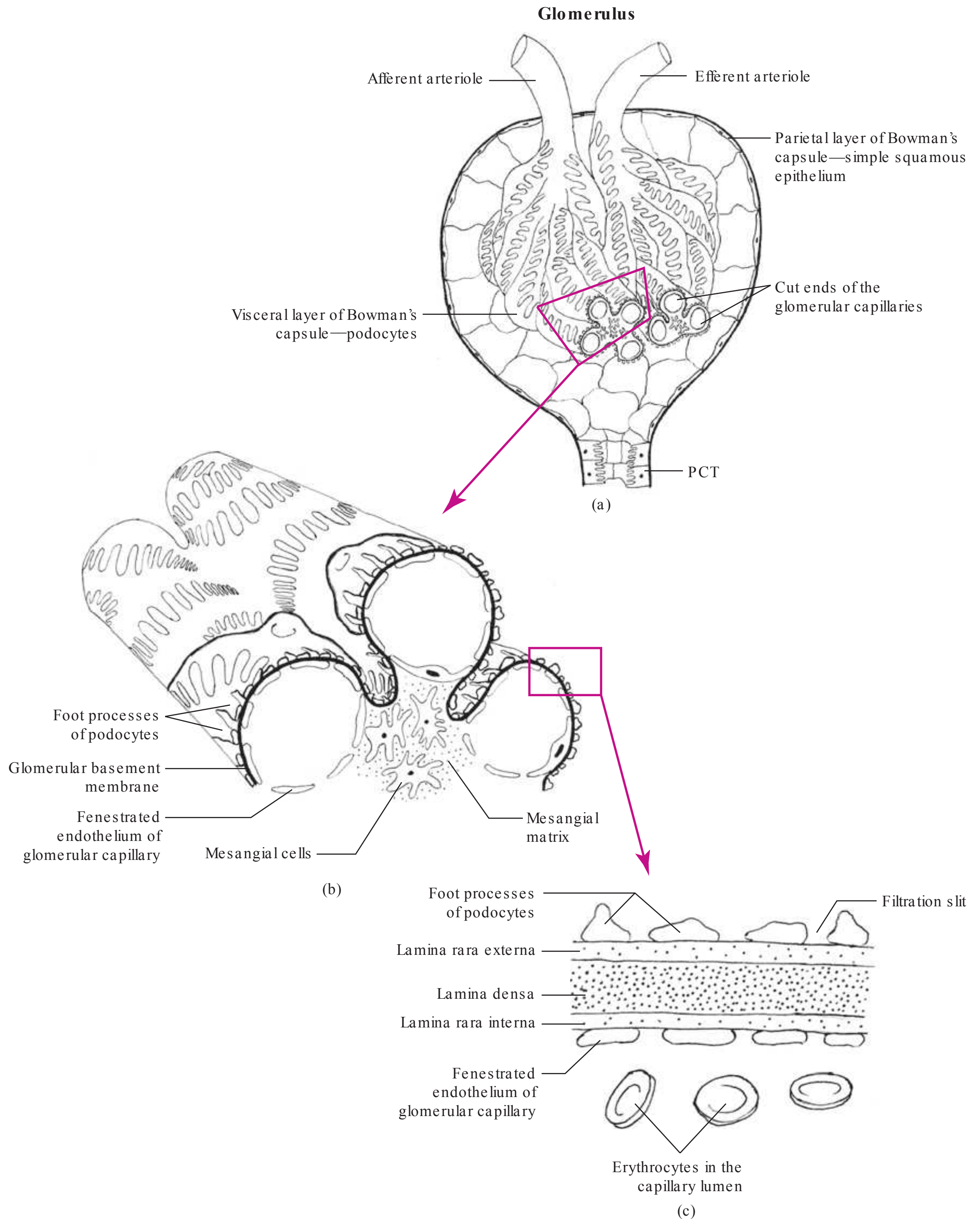
**Figure 16.7** Types of nephrons and their locations.

## ULTRASTRUCTURE OF RENAL CORPUSCLE

The ultrastructure of the renal corpuscle can be appreciated under an electron microscope.

### Mesangium

- In the glomerulus, in between the capillaries is the mesangium (Fig. 16.8).



**Figure 16.8** Schematic diagram of the renal corpuscle and its components. (a) Parietal and visceral layers of Bowman's capsule and glomerulus can be seen. (b) In between the glomerular capillaries, mesangium is seen which consists of mesangial cells and mesangial matrix. (c) Components of glomerular filtration barrier, which consists of endothelium of glomerular capillary, glomerular basement membrane and podocytes.



- The mesangium consists of mesangial cells and mesangial matrix. They provide structural support to the glomerulus.
- The components of the mesangium can be demonstrated by periodic acid–Schiff and methenamine silver stains.
- The mesangial cells are modified smooth muscle cells. They are irregular in shape and have numerous cytoplasmic processes. These cells have contractile properties due to the presence of actin, myosin and  $\alpha$ -actinin filaments. These cells also have phagocytic capabilities.
- The mesangial matrix consists of collagen, proteoglycans and glycoprotein (fibronectin).
- Functions: Structural support to the glomerulus and removal of the debris (aggregated macromolecules in glomerular basement membrane) by phagocytosis.

### Podocytes

- As described earlier, the visceral layer of Bowman's capsule is formed by podocytes (Fig. 16.8a).
- These cells give several extensions known as foot processes. The foot processes wrap around the capillary loops and interdigitate with the foot processes of the neighbouring podocytes (Fig. 16.8b).
- There are openings (30–40 nm wide) between the foot processes of the podocytes called filtration slits (Fig. 16.8c).

### Glomerular Basement Membrane

- Glomerular basement membrane (GBM) is common basal lamina of the capillary endothelium of the glomerulus and podocytes (Fig. 16.8b). It separates the foot processes of podocytes from the capillary endothelial cells and the mesangium.
- It is synthesised by both podocytes and capillary endothelial cells.
- Capillaries are not completely surrounded by the GBM; the GBM surrounds only the part of the capillary wall which is not in contact with the mesangium (Fig. 16.8b).
- It acts as a filtration barrier.
- It is demonstrated by periodic acid–Schiff and methenamine silver stains.
- The ultrastructure of the GBM shows that it consists of three layers: middle lamina densa, outer lamina rara externa which is in contact with the foot processes of podocytes and inner lamina rara interna which is in contact with the capillary endothelial cells and mesangium (Fig. 16.8c).
- The major component of the GBM is type IV collagen. The other components are glycosaminoglycans and glycoproteins (fibronectin and laminin).

### Glomerular Filtration Barrier

- The glomerular filtration barrier consists of the structures present between the blood in the glomerular capillary and the urinary space (Fig. 16.8c). These structures are as follows:
  - (a) Endothelium of the capillary, which is fenestrated
  - (b) GBM
  - (c) Podocytes
- This barrier acts as a selective barrier. The selectivity depends upon the size and the charge of the molecule. Small molecules pass through the filtration barrier and enter the urinary space; blood cells and large proteins are retained within the blood capillary.

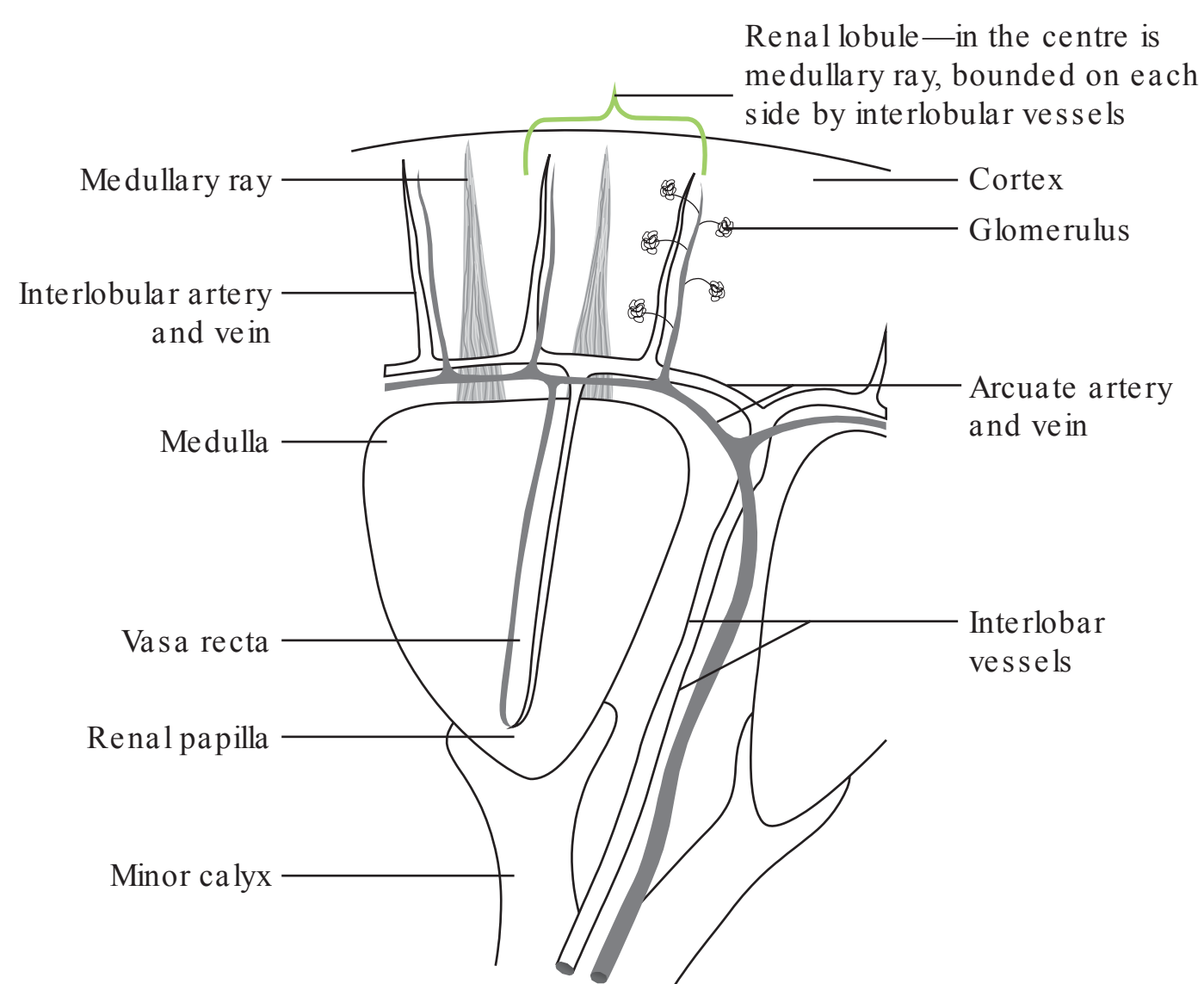
### Juxtaglomerular Apparatus (Fig. 16.6)

- It is present at the vascular pole of the renal corpuscle, where the DCT comes in contact with the afferent arteriole of the glomerulus.
- It is involved in regulation of blood pressure.
- It consists of macula densa, juxtaglomerular cells (JG cells) and lacis cells or extraglomerular mesangial cells (Fig. 16.6).

- JG cells are present in the wall of afferent arterioles of the glomerulus. They are modified smooth muscles and they secrete renin.
- Lacis cells are a group of cells present close to macula densa between afferent and efferent arterioles.
- The renin is released from the JG cells into the blood in response to reduced blood pressure or low sodium concentration in the fluid present in the distal tubule.
- The renin converts the angiotensinogen (synthesised in the liver) into angiotensin I. Angiotensin I is converted to angiotensin II by angiotensin-converting enzyme released from the endothelial cells of the lung capillary.
- Angiotensin II stimulates the cells of zona glomerulosa of the adrenal gland to release hormone aldosterone.
- Aldosterone acts on the distal tubule of the kidney and increases the resorption of sodium and water. As a result, blood pressure and blood volume increases.
- The cells of macula densa sense the  $\text{Na}^+$  concentration in the distal tubule and regulate the release of renin, and hence have a role in regulating the activity of juxtaglomerular apparatus.

### **BLOOD SUPPLY OF THE KIDNEY**

- Renal arteries enter the kidney through the hilum and divide into several branches. These branches give rise to the interlobar arteries which ascend between the pyramids towards the corticomedullary junction (Fig. 16.9).
- At the corticomedullary junction, the interlobar artery divides into arcuate arteries. Arcuate arteries run over the bases of the pyramid (Fig. 16.9).
- Arcuate arteries give rise to the interlobular arteries, which are present in the cortex on the sides of medullary ray (Fig. 16.9).
- Interlobular arteries give afferent arteriole to the glomerulus.
- Efferent arteriole of the cortical nephron forms the peritubular plexus around the PCT and DCT, and the peritubular plexus drains into the interlobular veins.
- Vasa recta: Efferent arteriole of the juxtamedullary nephron gives straight capillaries located in the medulla. They are closely associated with the loop of Henle, and these capillaries are called vasa recta; they drain into the arcuate veins.



**Figure 16.9** Diagram of kidney showing its blood vessels.



## URETER

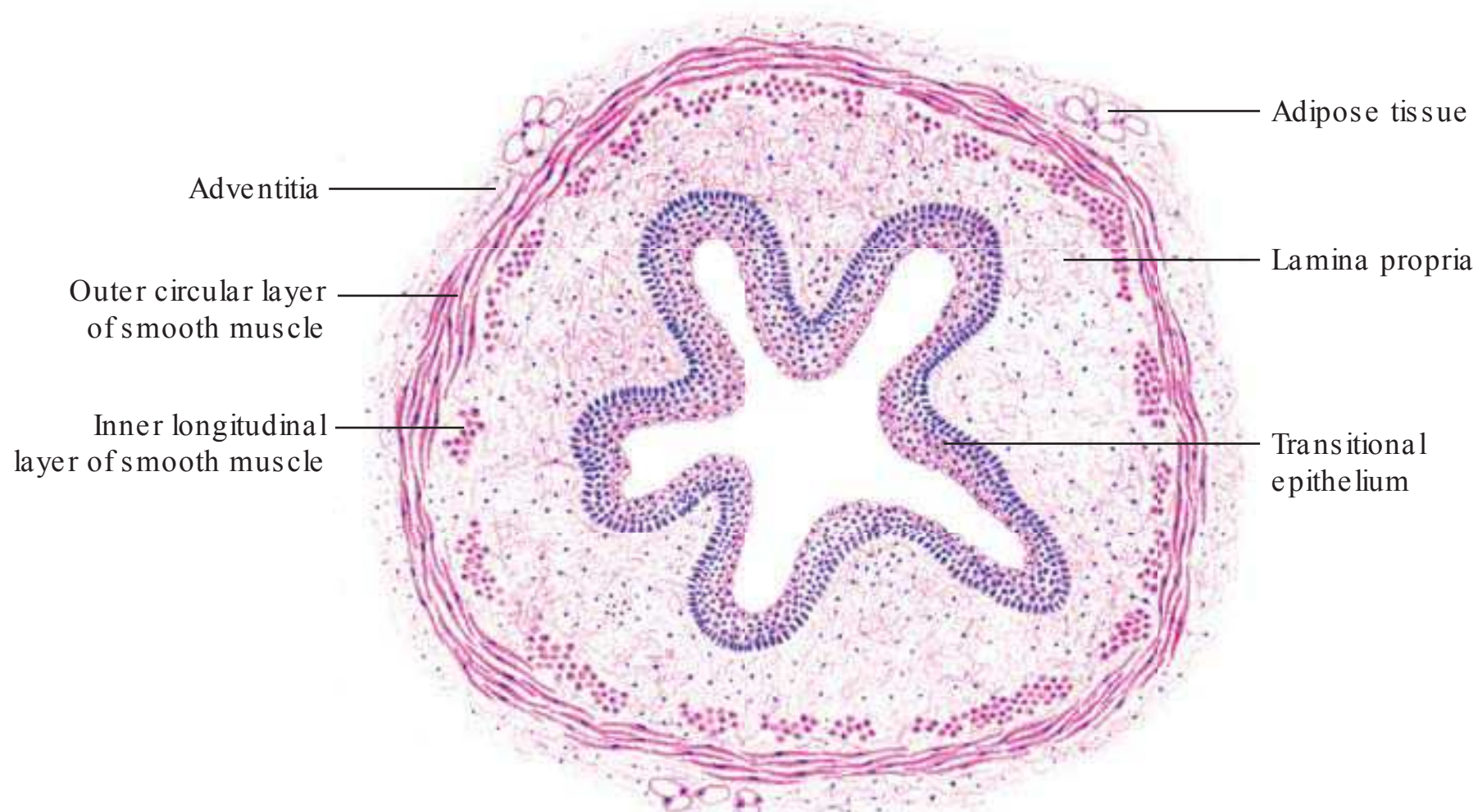
Ureters convey the urine from the renal pelvis to the urinary bladder.

### MICROSCOPIC STRUCTURE

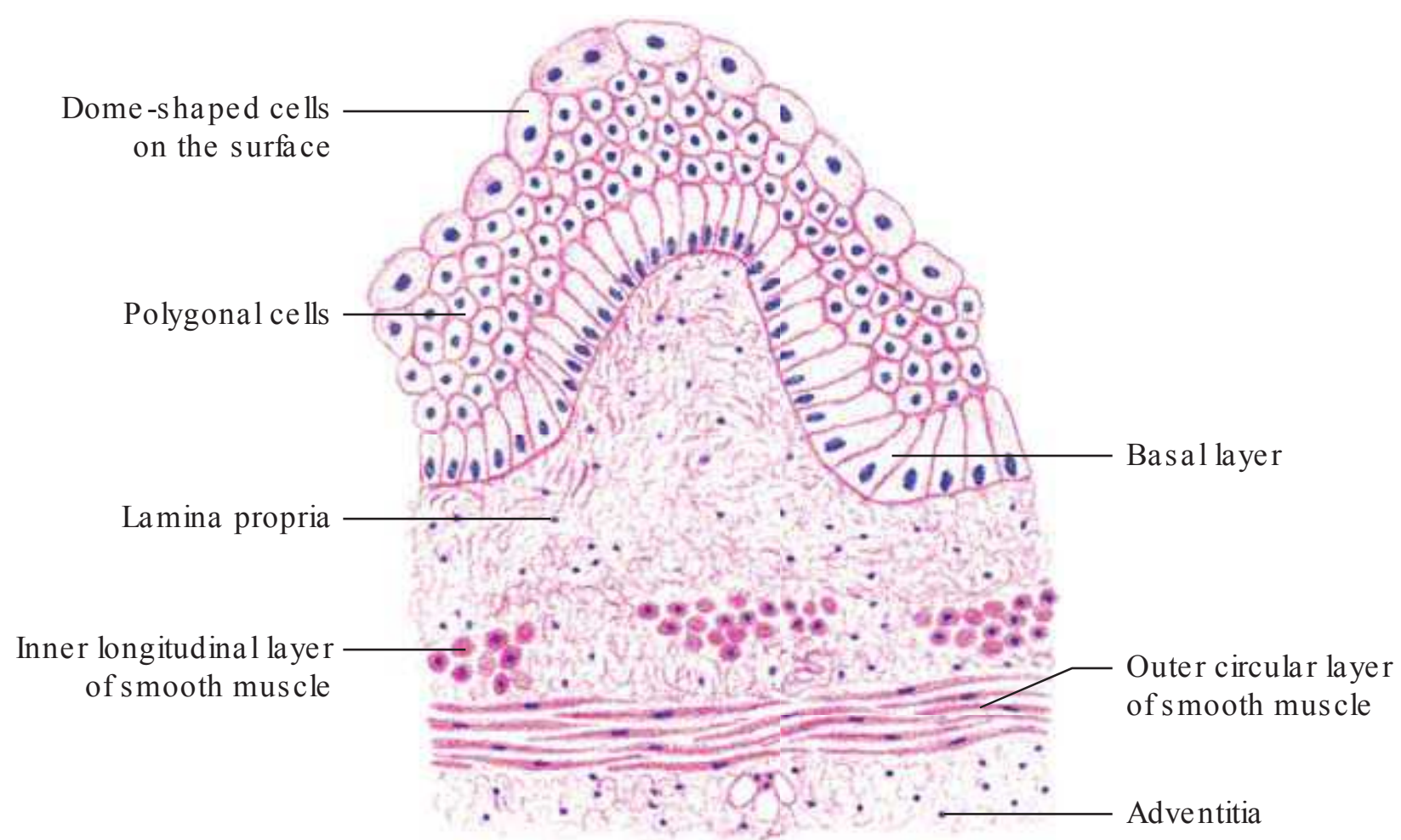
The wall of the ureter consists of mucosa, muscular layer and adventitia (Fig. 16.10; PMG 16.2 and 16.3).

#### Mucosa

- The mucosa is folded; the lumen appears 'star shaped' in the transverse section.
- Lining epithelium is transitional epithelium, and it is four to five layers thick.
- Underneath the epithelium is lamina propria.



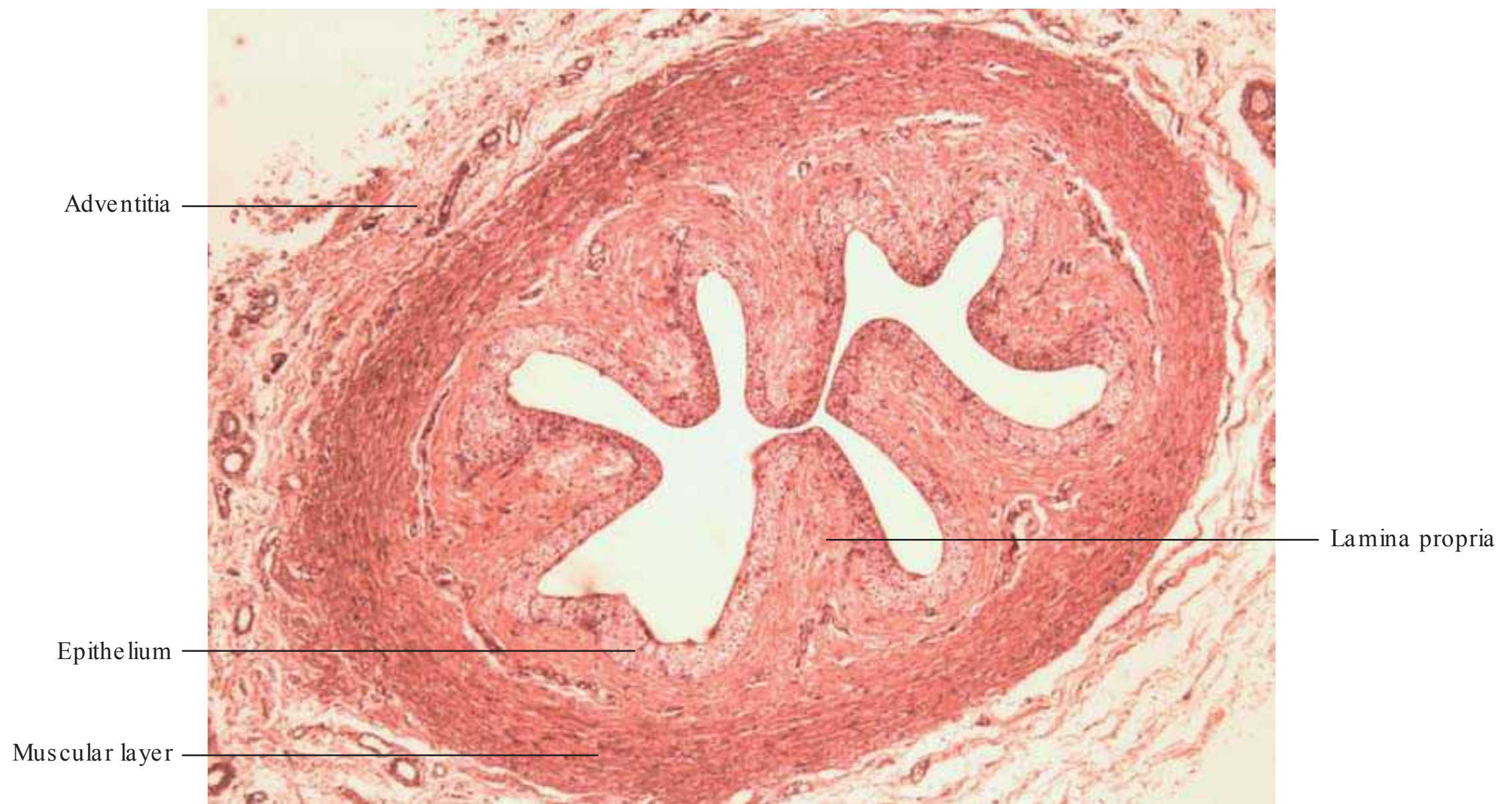
(a)



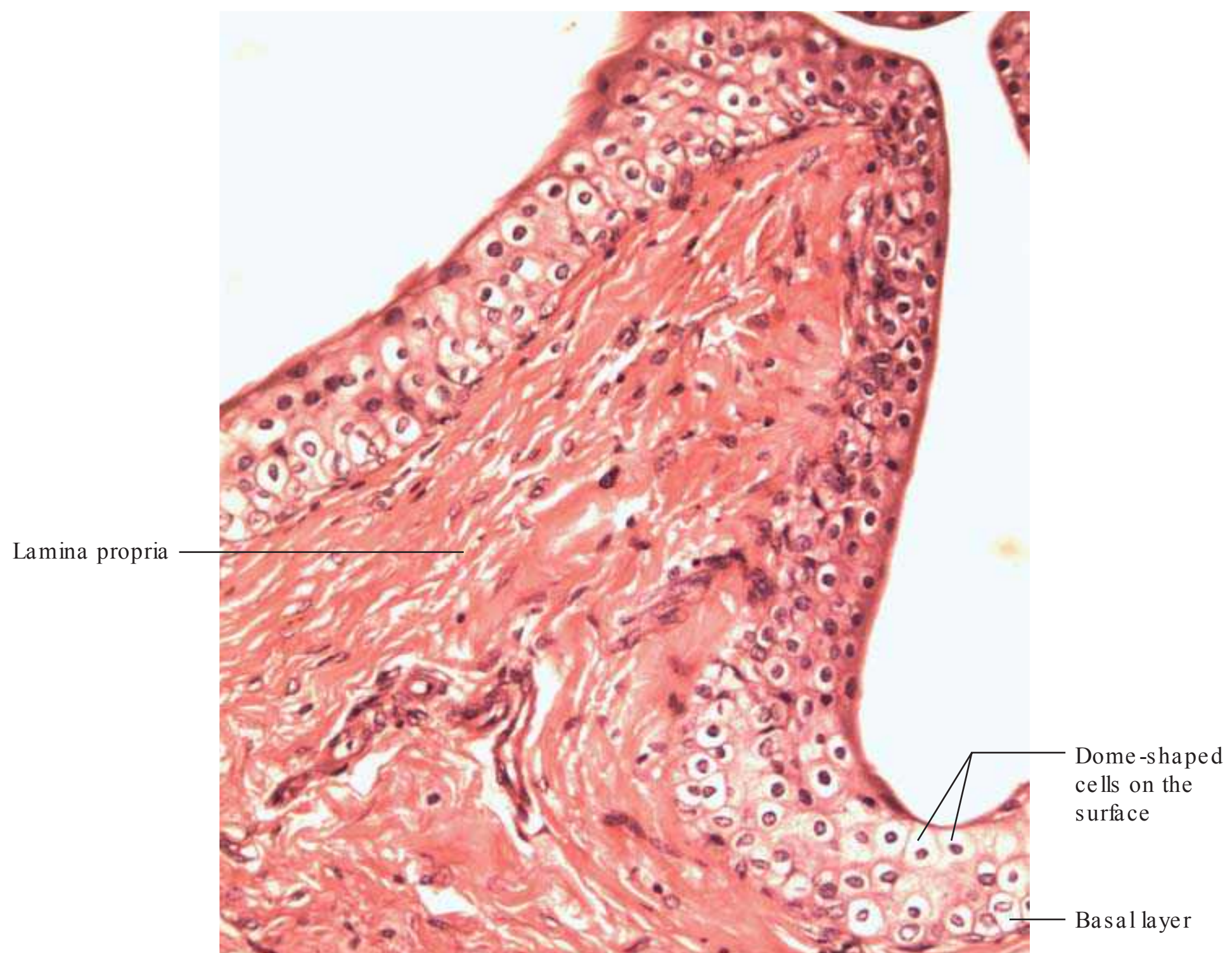
(b)

**Figure 16.10** Section of ureter in (a) low and (b) high magnification (H&E pencil drawing).





**PMG 16.2** Ureter (H&Estain, X5).



**PMG 16.3** Transitional epithelium of the ureter (H&Estain, X20).

### Muscular Layer

- It consists of inner longitudinal and outer circular layers of smooth muscles (note that the arrangement of smooth muscles in the gastrointestinal tract is inner circular and outer longitudinal layers).



- In the lower one-third, an additional outer longitudinal layer is present.
- Contractions of these muscles produce peristaltic movement which propels the urine into the urinary bladder.

### Adventitia

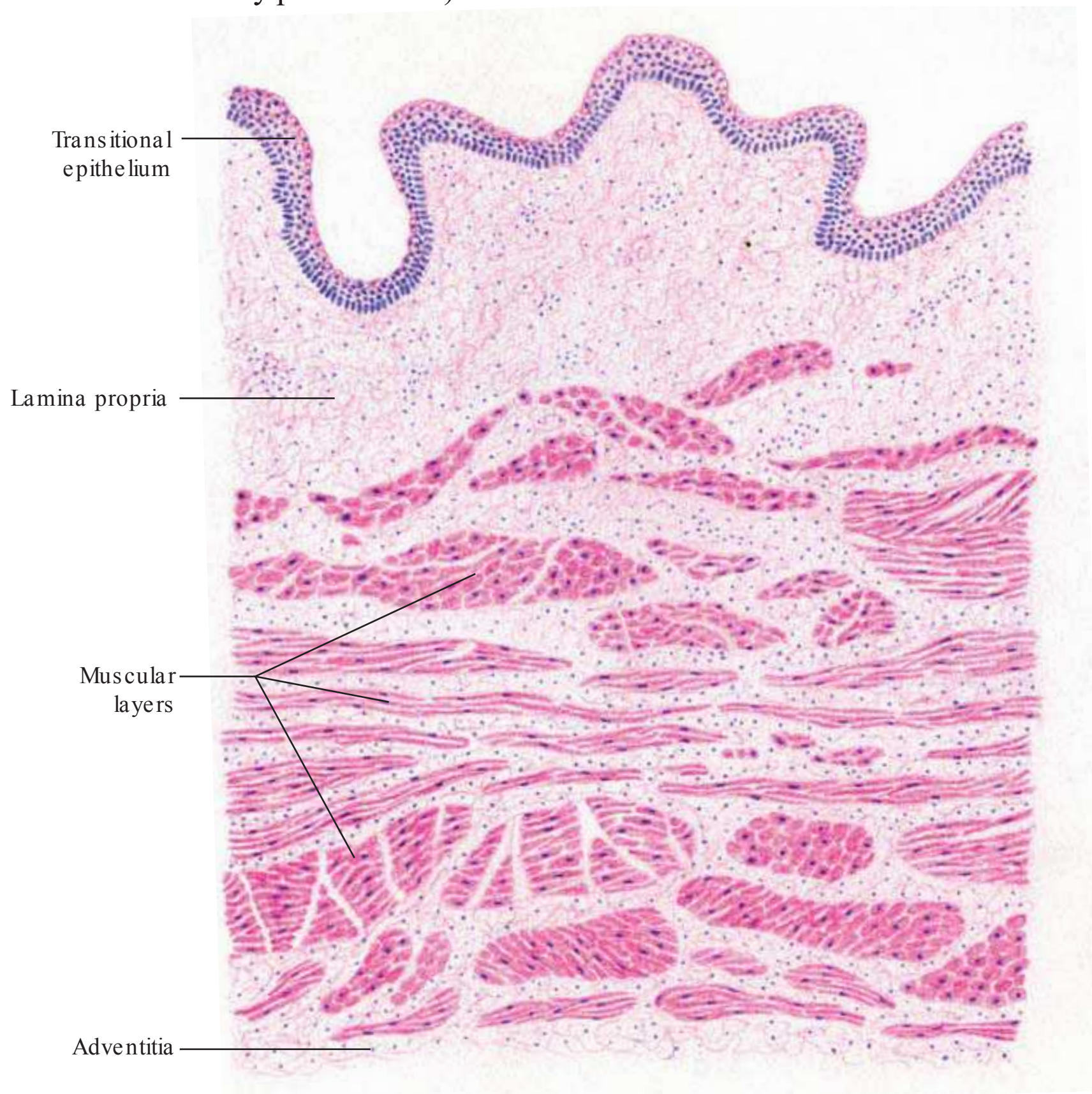
- It is the outermost layer.

## URINARY BLADDER

The urinary bladder is a distensible sac located in the pelvis. It stores urine temporarily.

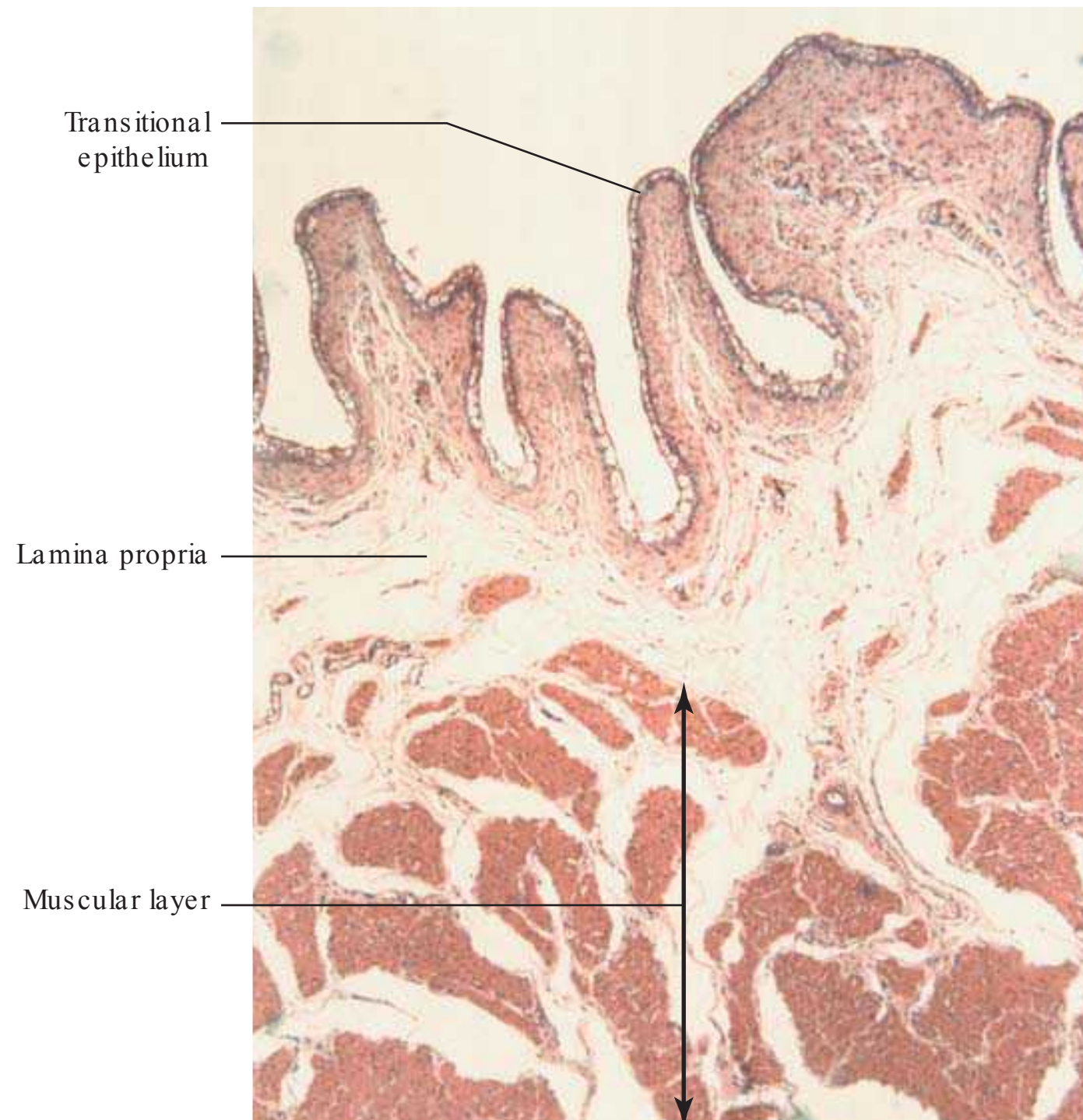
### MICROSCOPIC STRUCTURE

- The structure of the wall of the urinary bladder is almost same as the lower one-third of the ureter. The bladder wall is thicker than the ureter. In the relaxed state, the mucosa is highly folded; the epithelium is five to six layers thick (Fig. 16.11; PMG 16.4).
- The muscular layer forms the detrusor muscle. It consists of three layers of smooth muscles, as in the lower one-third of the ureter, i.e. middle circular, inner and outer longitudinal layers. Near the urethral opening of the urinary bladder, the smooth muscles are arranged circularly to form internal urethral sphincter; it is involuntary in function.
- Adventitia is the outermost layer except in the upper part of the bladder where the outermost layer is serosa (since it is covered by peritoneum).



**Figure 16.11** Section of urinary bladder in low magnification (H&E pencil drawing).





**PMG 16.4** Urinary bladder (H&Estain, X5).

## URETHRA

- The urethra conveys the urine from the urinary bladder to the exterior.

### MICROSCOPIC STRUCTURE

- The wall of the urethra consists of epithelium, lamina propria and muscular layer.
- The type of epithelium varies within the urethra. Lamina propria has numerous mucus-secreting glands (glands of Littre).
- The muscular layer consists of an inner longitudinal and an outer circular layer of smooth muscles.

### Male Urethra

- It consists of three parts: prostatic part (in the prostate), membranous part (in the urogenital diaphragm) and penile part (in the corpus spongiosum of the penis) (Fig. 17.1, page 250).
- The prostatic part of the urethra is lined by transitional epithelium. Other parts of the male urethra are lined by pseudostratified or stratified columnar epithelium, except at the distal end where it changes to stratified squamous epithelium.
- The membranous part of the urethra is surrounded by skeletal muscles of the urogenital diaphragm to form the external urethral sphincter; it is voluntary in function.

### Female Urethra

- At the beginning (near the internal urethral orifice), it is lined by transitional epithelium; the remaining urethra is lined by stratified squamous epithelium.



## CLINICAL CORRELATES

### Glomerular Diseases

- A number of different diseases can result in glomerular disease. It may be due to an infection or a drug toxic to the kidneys, or it may result from a disease that affects the entire body, such as diabetes or systemic lupus erythematosus. Various histological changes can be seen in the glomerulus such as leucocytic infiltration, thickening of basement membrane and deposition of immune complex.

### Nephrotic Syndrome

- In this condition, the glomerular basement membrane becomes leaky which results in proteinuria, hypoalbuminaemia and oedema.

### Acute Nephritic Syndrome

- In this condition, there is haematuria, proteinuria, oedema and hypertension.

### Bladder Cancer

- Most of the bladder cancers arise from the epithelium. Haematuria is the most common symptom.

## KEYPOINTS

### Kidney (Figs 16.4 and 16.5; PMG 16.1)

Parts of the kidney	Parts of the nephron	Microscopic feature	Function
Cortex	Renal corpuscle	<ul style="list-style-type: none"><li>It consists of Bowman's capsule and glomerulus</li><li>The parietal layer of Bowman's capsule is lined by simple squamous epithelium and the visceral layer consists of podocytes</li></ul>	Glomerular filtration
	Proximal convoluted tubule (PCT)	<ul style="list-style-type: none"><li>It is lined by simple cuboidal cells with brush border</li></ul>	Reabsorption of glomerular filtrate
	Distal convoluted tubule (DCT)	<ul style="list-style-type: none"><li>It is lined by simple cuboidal cells without brush border</li></ul>	Reabsorption of sodium ions
Medulla	Loop of Henle	<ul style="list-style-type: none"><li>Thick part is lined by cuboidal epithelium</li><li>Thin part is lined by squamous epithelium</li></ul>	Sets up a gradient in osmotic pressure from the cortex to the medulla, which serves as driving force in the further concentration of the urine
	Vasa recta	<ul style="list-style-type: none"><li>Same as small blood vessels (Fig. 16.9)</li></ul>	
	Collecting tubule	<ul style="list-style-type: none"><li>It is lined by pale stained cuboidal cells</li></ul>	Reabsorption of water under the influence of the antidiuretic hormone (ADH)
	Collecting duct	<ul style="list-style-type: none"><li>Smaller ducts have cuboidal cells</li><li>Larger ducts have columnar cells</li></ul>	

### Excretory Passages

Except in urethra, the walls of the excretory passages have similar organisation. They consist of mucosa, muscular layer and adventitia (from lumen to outside), and the lining epithelium is transitional.

Wall structure	Excretory passage except urethra	Male urethra
Mucosa	<ul style="list-style-type: none"><li>Epithelium is transitional (ureter—Fig. 16.10; PMG 16.2 and 16.3; urinary bladder—Fig. 16.11; PMG 16.4)</li></ul>	<ul style="list-style-type: none"><li>Epithelium varies:<ul style="list-style-type: none"><li>(a) Prostatic part—transitional epithelium</li><li>(b) Remaining parts except the distal end—pseudostratified or stratified columnar epithelium</li><li>(c) Distal end—stratified squamous epithelium</li></ul></li></ul>
Muscular layer (smooth muscles)	<ul style="list-style-type: none"><li>Upper two-thirds of ureter—inner longitudinal and outer circular layers (Fig. 16.10)</li><li>Lower one-third of ureter and urinary bladder—middle circular and inner and outer longitudinal layers (Fig. 16.11)</li></ul>	<ul style="list-style-type: none"><li>Inner longitudinal and outer circular layer</li></ul>

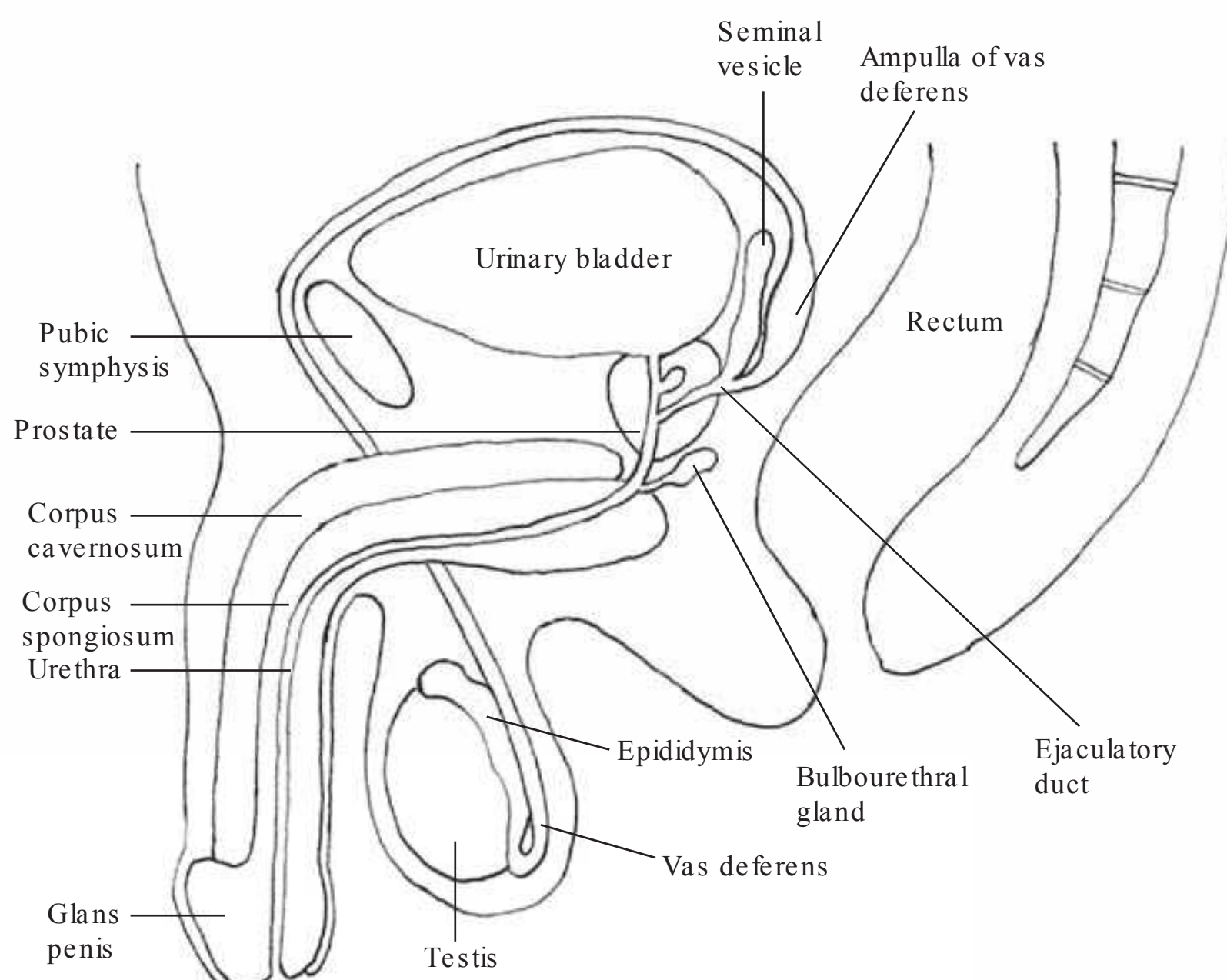
SELF-ASSESSMENT

- Describe the structure of a renal corpuscle.
- What are the parts of a nephron? Name the type of cells lining the different parts of a nephron.
- What are the different types of nephrons?
- What are the components of the cortex and the medulla of a kidney?
- What is a renal lobe?
- Where is the juxtaglomerular apparatus located? What are the different types of cells present in it?
- What is the lining epithelium of the ureter and the urinary bladder?



# Male Reproductive System

- The male reproductive system consists of testes (singular: testis), duct system, accessory glands and penis (Fig. 17.1).
- Spermatozoa are produced in the testis and are carried by the duct system to the exterior. The duct system includes epididymis, vas deferens, ejaculatory duct and part of urethra.
- Accessory glands are seminal vesicles, prostate and bulbourethral glands.



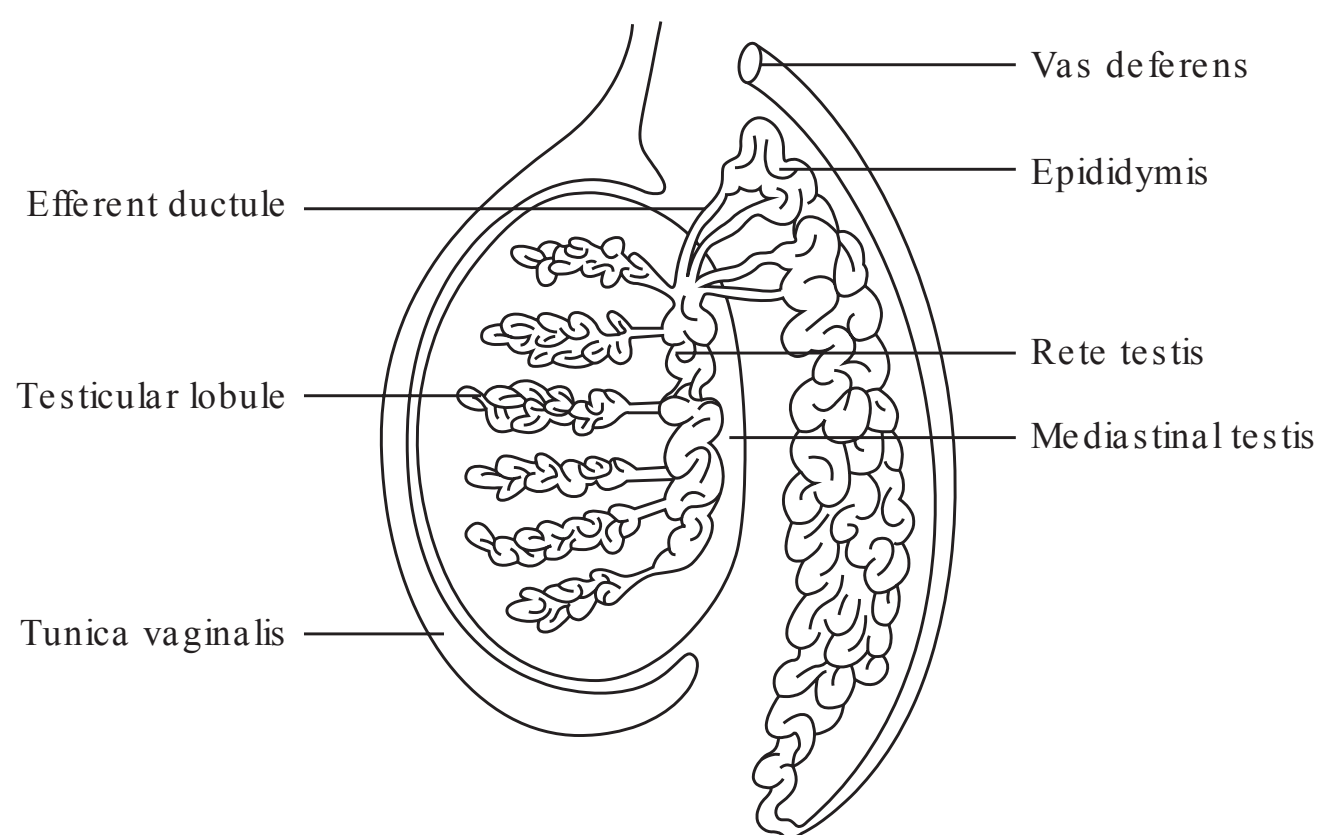
**Figure 17.1** Male reproductive system (lateral view).

## TESTIS

- Testes are a pair of male gonads located in the scrotum. The testis develops in the posterior abdominal wall and descends into the scrotum. The temperature of the scrotum is 2–3°C lower than the body temperature, which is essential for normal spermatogenesis.
- The testes have two functions: production of the male gametes and synthesis and secretion of the male sexual hormone testosterone.

### STRUCTURAL ORGANISATION (Fig. 17.2)

- Coverings of testis from outside inwards are tunica vaginalis, tunica albuginea and tunica vasculosa.
- Tunica vaginalis is a serous sac covering the entire testis except the posterior border (Fig. 17.2).
- Tunica albuginea is dense connective tissue surrounding the testis. At the posterior border of the testis, it enters the testis and forms mediastinum testis. From the mediastinum testis, numerous septa extend into the substance of the testis and divide it into about 250 lobules (Fig. 17.2).
- Tunica vasculosa is a vascular layer which lines the individual lobules of testis.
- Each lobule contains one to four seminiferous tubules, loose connective tissue and interstitial cells of Leydig.
- Seminiferous tubules of adjacent lobules join to form a network of tubules called rete testis. Twelve to eighteen efferent ductules arise from the rete testis and enter the head of epididymis (Fig. 17.2).

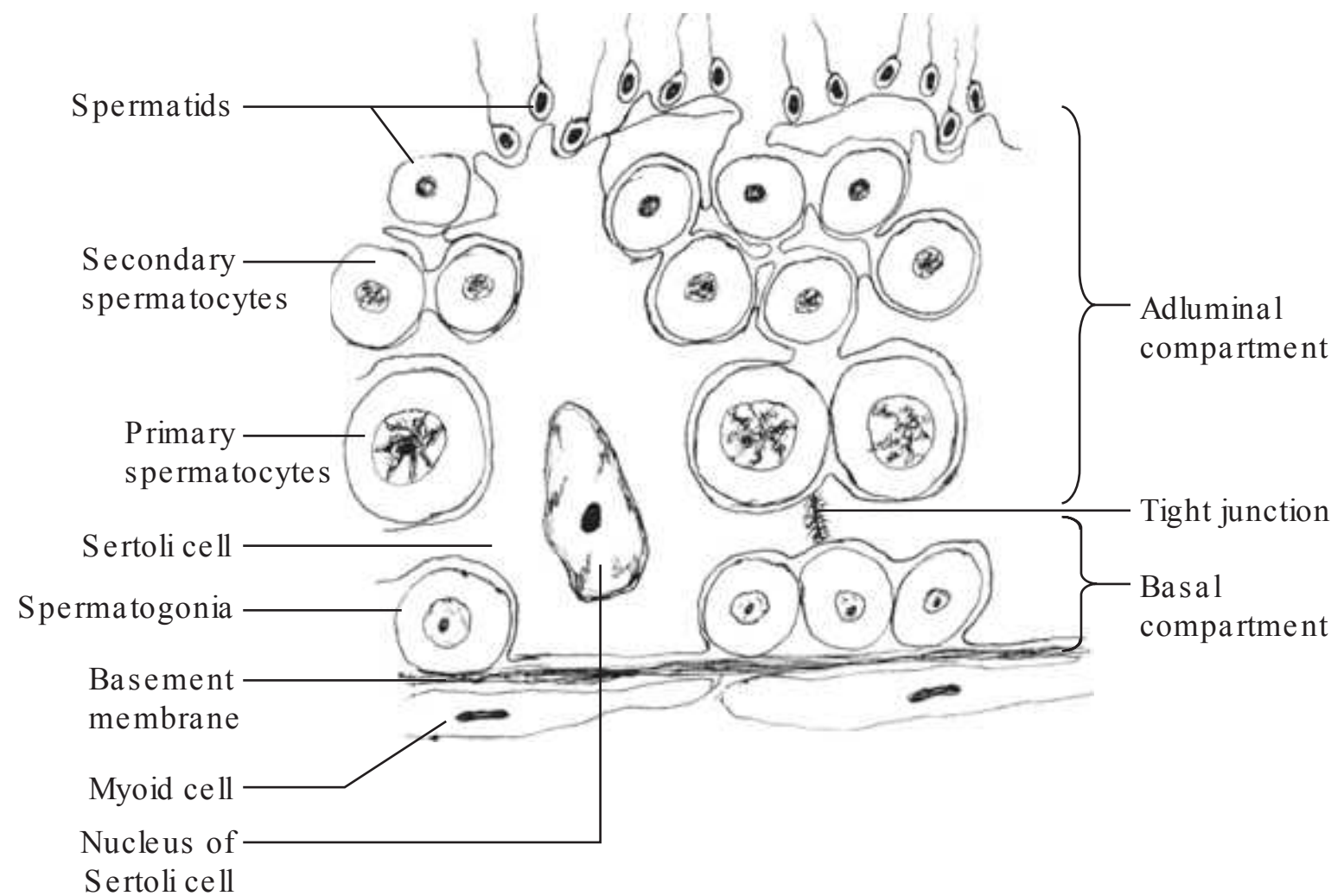


**Figure 17.2** Structural organisation of the testis and epididymis.

### Seminiferous Tubules

- Seminiferous tubules are highly convoluted tubules.
- The interior of the tubules is lined with stratified seminiferous epithelium (Fig. 17.3), which consists of two types of cells: spermatogenic cells and Sertoli cells. Spermatogenic cells divide and differentiate into sperms. Sertoli cells are the supporting cells. Cells in different stages of spermatogenesis can be seen.
- The cells rest on a thick basement membrane. Outside the basement membrane, the tubules are surrounded by a few layers of cells structurally similar to smooth muscle cells (myoid cells) (Fig. 17.3).





**Figure 17.3** Stratified seminiferous epithelium. Spermatogenic cells in various stages of development along with supporting Sertoli cells can be seen.

### *Spermatogenic Cells* (Fig. 17.3; also see Fig. 17.4)

- Spermatogenic cells are discussed as follows:
  - (a) Spermatogonia: They are always in contact with the basement membrane of the tubule. These cells have diploid number of chromosomes.
  - (b) Primary spermatocytes: They are the largest germ cells; their location is more luminal than the spermatogonia. The chromatin in the nucleus of these cells appears as clumps or thin threads; these cells have diploid number of chromosomes.
  - (c) Secondary spermatocytes: They are smaller than the primary spermatocytes. Their location is more luminal than primary spermatocytes. Since secondary spermatocytes enter and complete the second meiotic division rapidly, it is difficult to see these cells in histological preparations. These cells have haploid number of chromosomes.
  - (d) Spermatids: They lie next to the lumen and have haploid number of chromosomes.
  - (e) Spermatozoa (singular: spermatozoon): They are located in the lumen and have large flagella.

### *Sertoli Cells*

- Sertoli cells are pyramid-shaped cells with ovoid nuclei. They extend from the basement membrane to the lumen of the seminiferous tubule (Fig. 17.3).
- The basal parts of Sertoli cells have numerous processes on the lateral surfaces. These processes of adjacent Sertoli cells are interconnected by tight junctions.
- These tight junctions of the Sertoli cells are responsible for the blood–testis barrier.
- Tight junctions interconnecting the Sertoli cells divide the lumen of the seminiferous tubule into basal and adluminal compartments. In the basal compartment, spermatogonia are present, whereas other cells are present in the adluminal compartment (Fig. 17.3).
- Functions
  - (a) Mechanical and nutritive support to spermatogenic cells
  - (b) Phagocytosis of residual bodies: Residual bodies consist of the cytoplasm which is shed by spermatids during spermiogenesis (described later in the chapter)
  - (c) Secretion of androgen-binding protein, inhibin and Mullerian-inhibiting substance (MIS): Androgen-binding protein is responsible for maintaining the required concentration of testosterone in the seminiferous tubules which is essential for spermatogenesis. Androgen-binding protein is

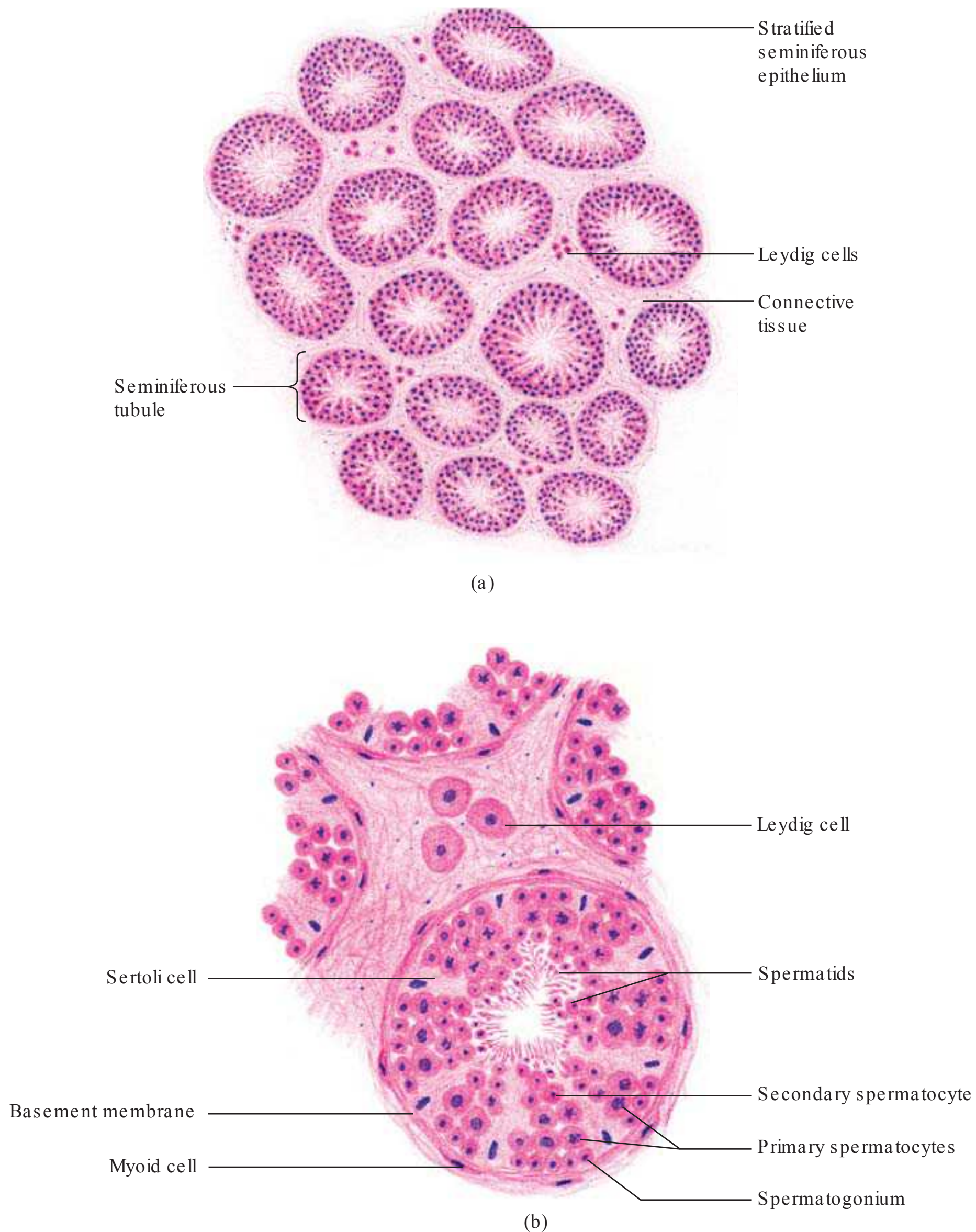


under control of follicle-stimulating hormone (FSH) secreted from pituitary. Inhibin inhibits the synthesis of FSH in anterior pituitary. MIS is secreted from Sertoli cells in developing foetus, and it suppresses further development of the Mullerian ducts (paramesonephric ducts)

(d) Blood–testis barrier formation

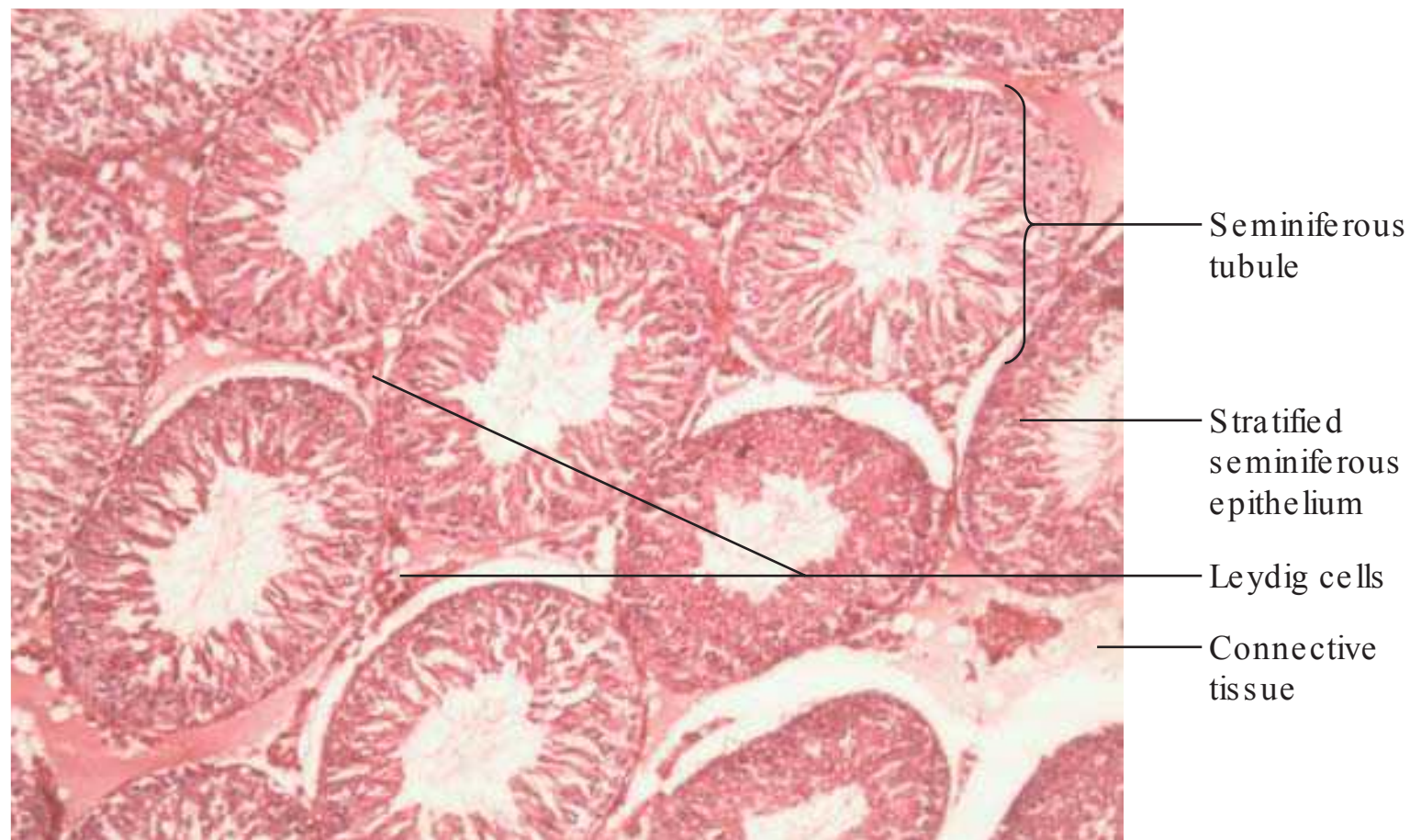
### Leydig Cells

- Leydig cells are located in the connective tissue between the seminiferous tubules.
- These are polygonal cells with round nuclei and are present in clusters (Fig. 17.4; PMG 17.1).
- They constitute the endocrine part of the testis; they synthesise and secrete testosterone.



**Figure 17.4** Section of testis in (a) low and (b) high magnification (H&E pencil drawing).

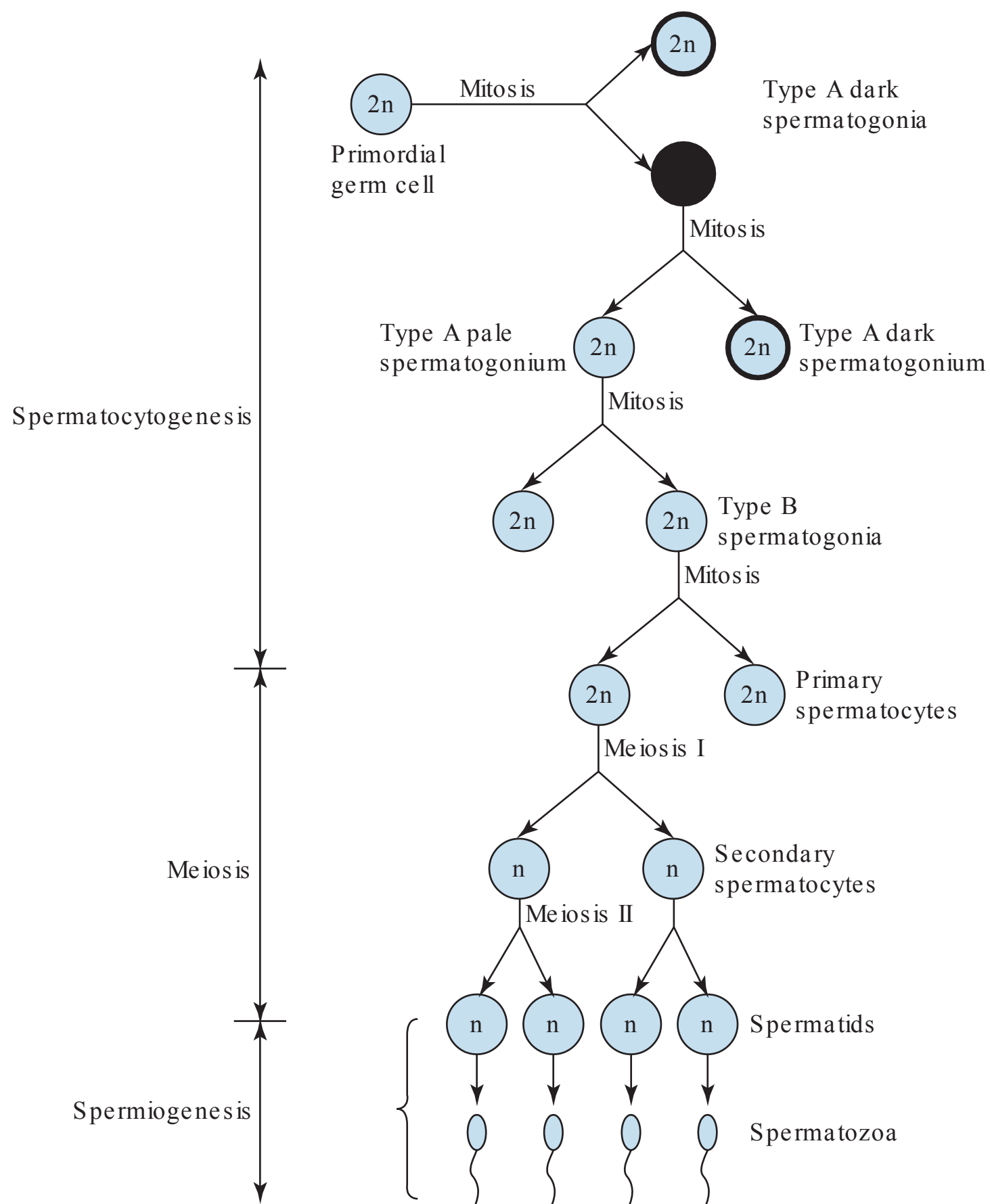




**PMG 17.1** Testis (H&Estain, X10).

## SPERMATOGENESIS

It is subdivided into three stages: spermatocytogenesis, meiosis and spermiogenesis (Fig. 17.5).



**Figure 17.5** Spermatogenesis. 2n denotes diploid and n denotes haploid number of chromosomes.

## Spermatocytogenesis

- Primordial germ cells migrate from the yolk sac to the testes in the fourth week of foetal development. They remain dormant until puberty. At puberty these cells differentiate into type A dark spermatogonia, which have a dark-staining nucleus.
- Type A spermatogonia undergo mitotic division to produce more type A dark spermatogonia and type A pale spermatogonia. Type A pale spermatogonia have a pale-staining nucleus.
- Type A pale spermatogonia differentiate into type B spermatogonia. Type B spermatogonia divide to produce primary spermatocytes.
- Till this stage all cells have diploid number ( $2n$ ) of chromosomes.

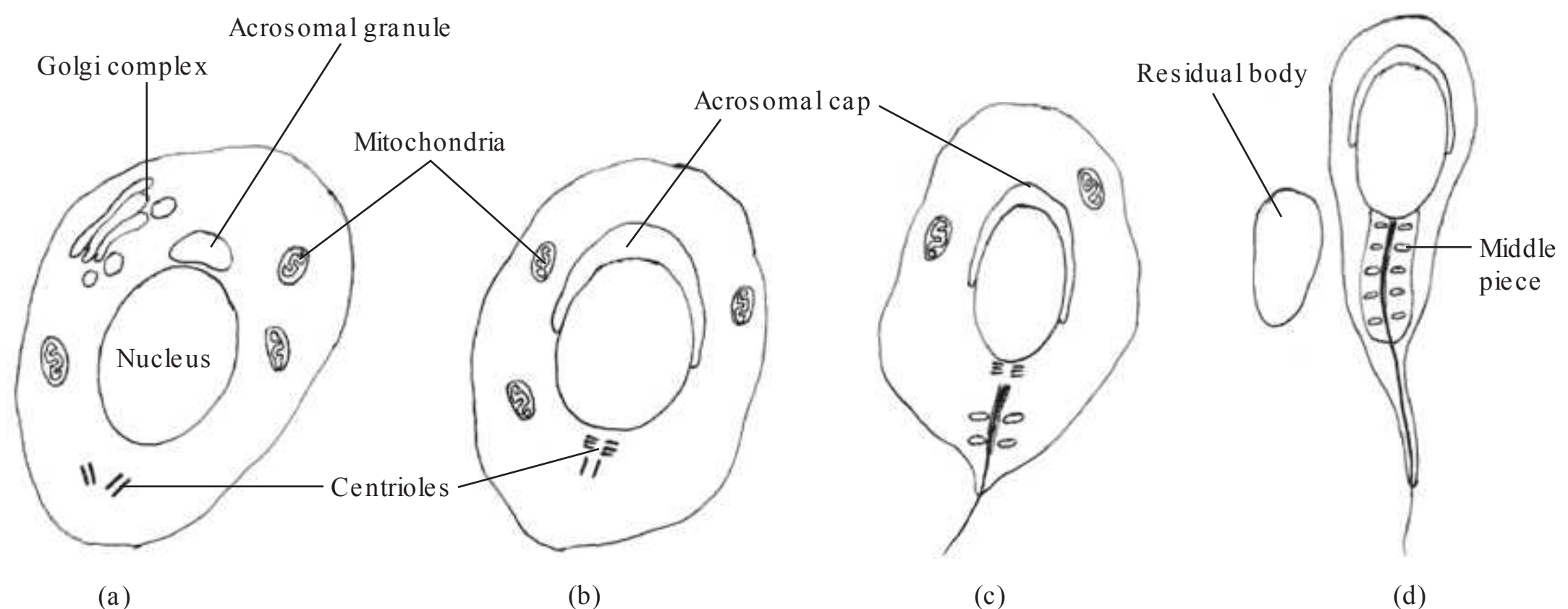
## Meiosis

- Primary spermatocytes enter meiosis I and produce haploid ( $n$ ) secondary spermatocytes.
- After this stage all daughter cells have haploid number of chromosomes.
- Secondary spermatocytes enter meiosis II and produce spermatids.

## Spermiogenesis

- During this process, spermatids undergo a series of morphological changes to form spermatozoa; no cell division takes place during this stage.
- These morphological changes occur in four phases: Golgi phase, cap phase, acrosomal phase and maturation phase.

- (a) Golgi phase: Acrosomal granules appear in Golgi complexes. These granules are enclosed in membrane-bound acrosomal vesicle. Acrosomal vesicle gets attached to one pole of the nucleus; this becomes the anterior pole of spermatozoa (Fig. 17.6a and b). Centrioles migrate to the posterior pole of the nucleus; the distal centriole gets aligned at right angle to the plasma membrane and begins the formation of axoneme of the tail of spermatozoa (Fig. 17.6b).
- (b) Cap phase: Acrosomal vesicle enlarges and covers two-thirds of the nucleus (Fig. 17.6c).
- (c) Acrosomal phase: The nucleus becomes condensed. Mitochondria are aggregated in a spiral manner around the proximal part of the tail—this region is the middle piece (Fig. 17.6d). The orientation of the spermatid changes; the anterior pole is directed towards the base and the developing tail towards the lumen of the seminiferous tubule.
- (d) Maturation phase: The excess cytoplasm is shed as residual body (Fig. 17.6d), which is phagocytosed by Sertoli cells.

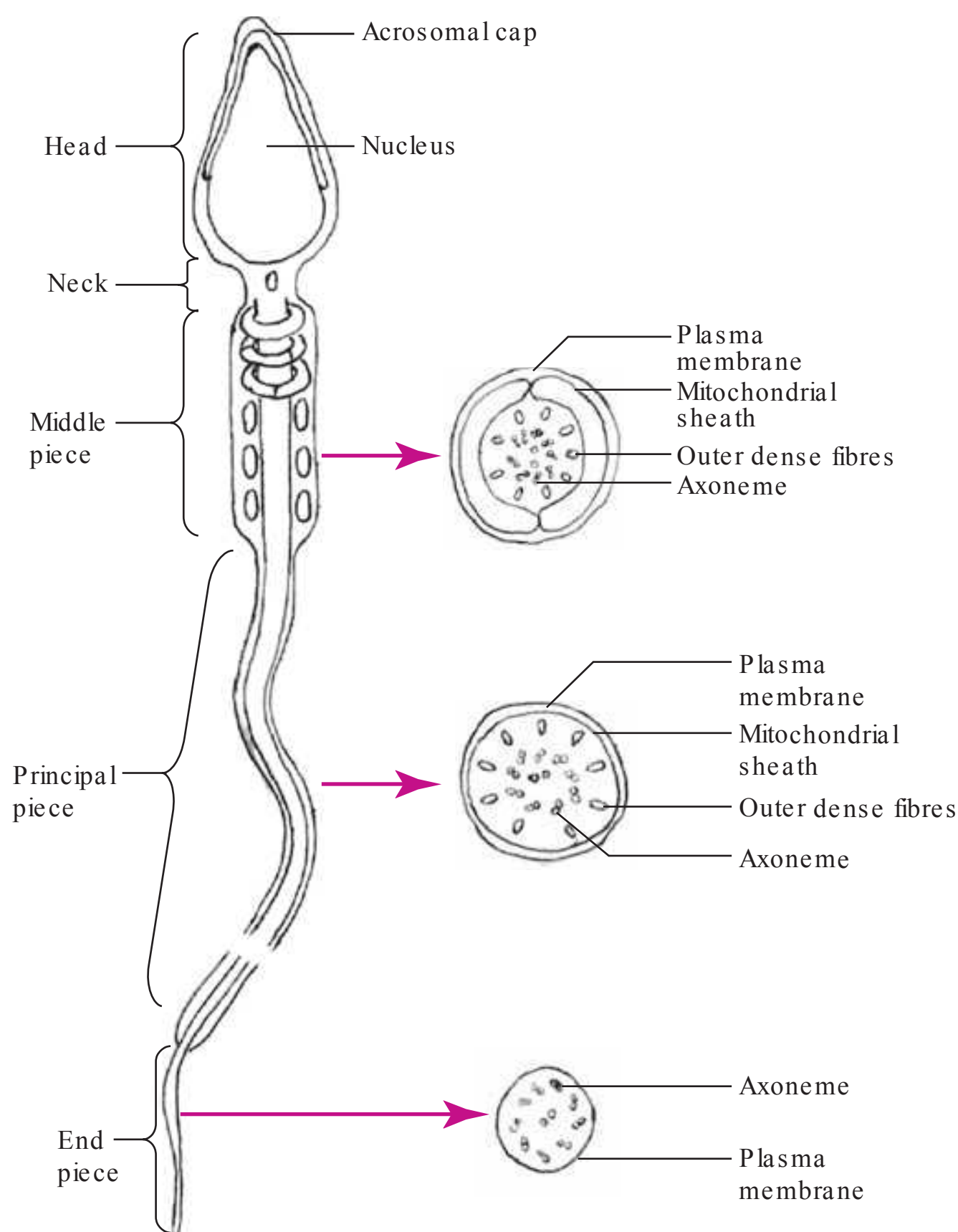


**Figure 17.6** Spermiogenesis. Morphological changes occurring in the spermatid in (a and b) Golgi phase, (c) cap phase and (d) acrosomal and maturation phases can be seen.



**STRUCTURE OF MATURE SPERMATOZOON (Fig. 17.7)**

- A mature spermatozoon (or sperm) consists of head, neck and tail.
- The head chiefly consists of the nucleus; anterior two-thirds of the nucleus is covered by the acrosome. The acrosome contains numerous enzymes, which facilitate penetration into the corona radiata and zona pellucida of the oocyte during fertilisation.
- Neck connects the head with the tail. It contains centrioles, connecting piece (basal plate) and the origin of nine outer dense fibres which continue in the tail.
- The tail is further divided into a middle piece, a principal piece and an end piece. The axoneme is present in the centre of the entire tail and consists of '9 + 2' arrangement of microtubules.
- Middle piece contains the axoneme in the centre surrounded by the nine outer dense fibres. External to these dense fibres, mitochondria are arranged in a helix. Mitochondria provide the energy required for the movement of the tail.
- Principal piece is the longest part of the tail. It also contains the axoneme surrounded by the nine outer dense fibres; in addition, it contains a sheath of circumferential fibres outside the dense fibres.
- End piece consists of only the axoneme surrounded by plasma membrane.



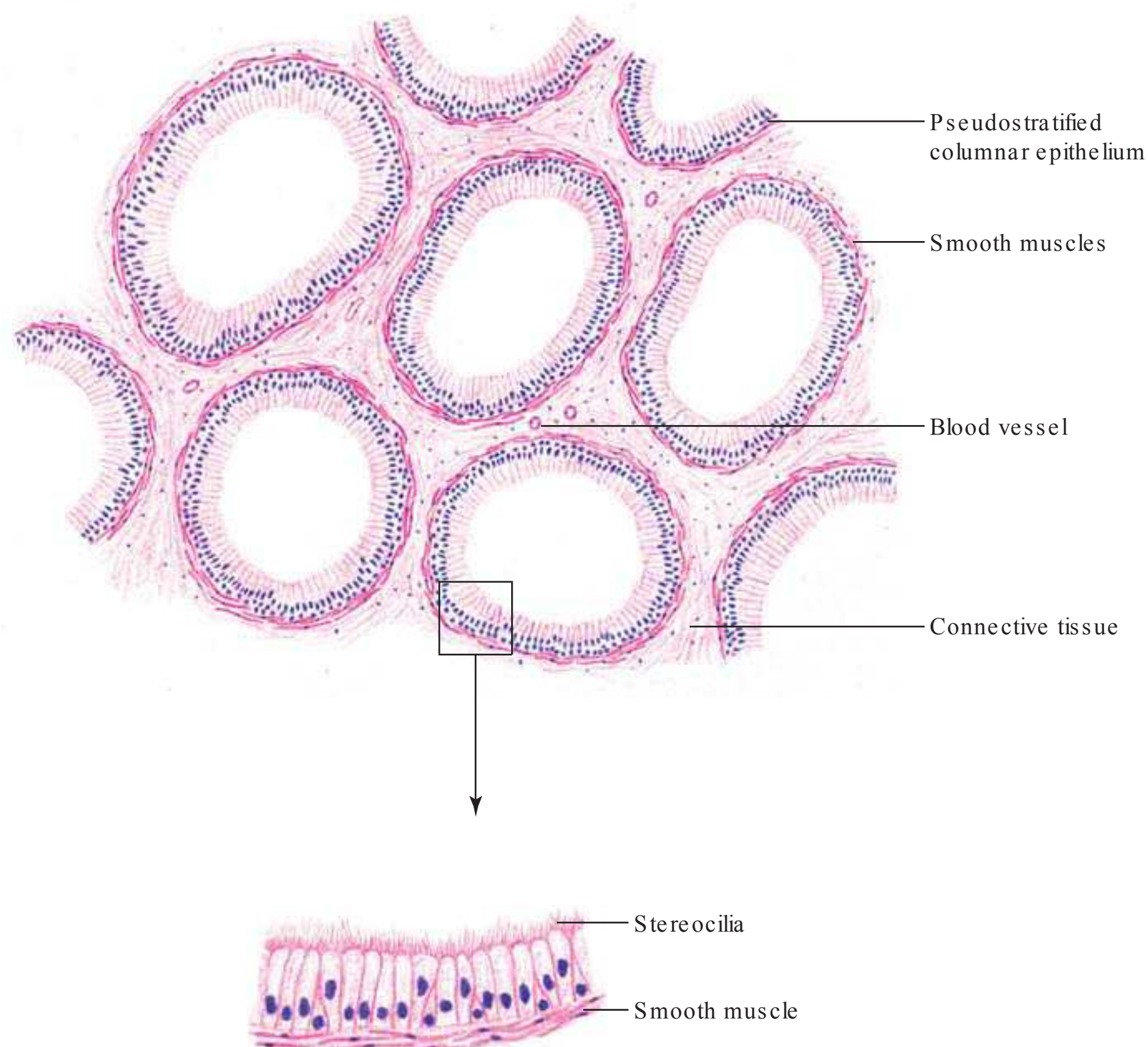
**Figure 17.7** A mature spermatozoon. Right: Enlarged view of the transverse section of middle, principal and end pieces.

## EPIDIDYMIS

- Epididymis is a single, long and extremely convoluted duct located at the posterior aspect of each testis (Fig. 17.1).
- It consists of a head, which receives efferent ductules, a body and a tail, which is at the lower pole of the testis and continues as vas deferens.

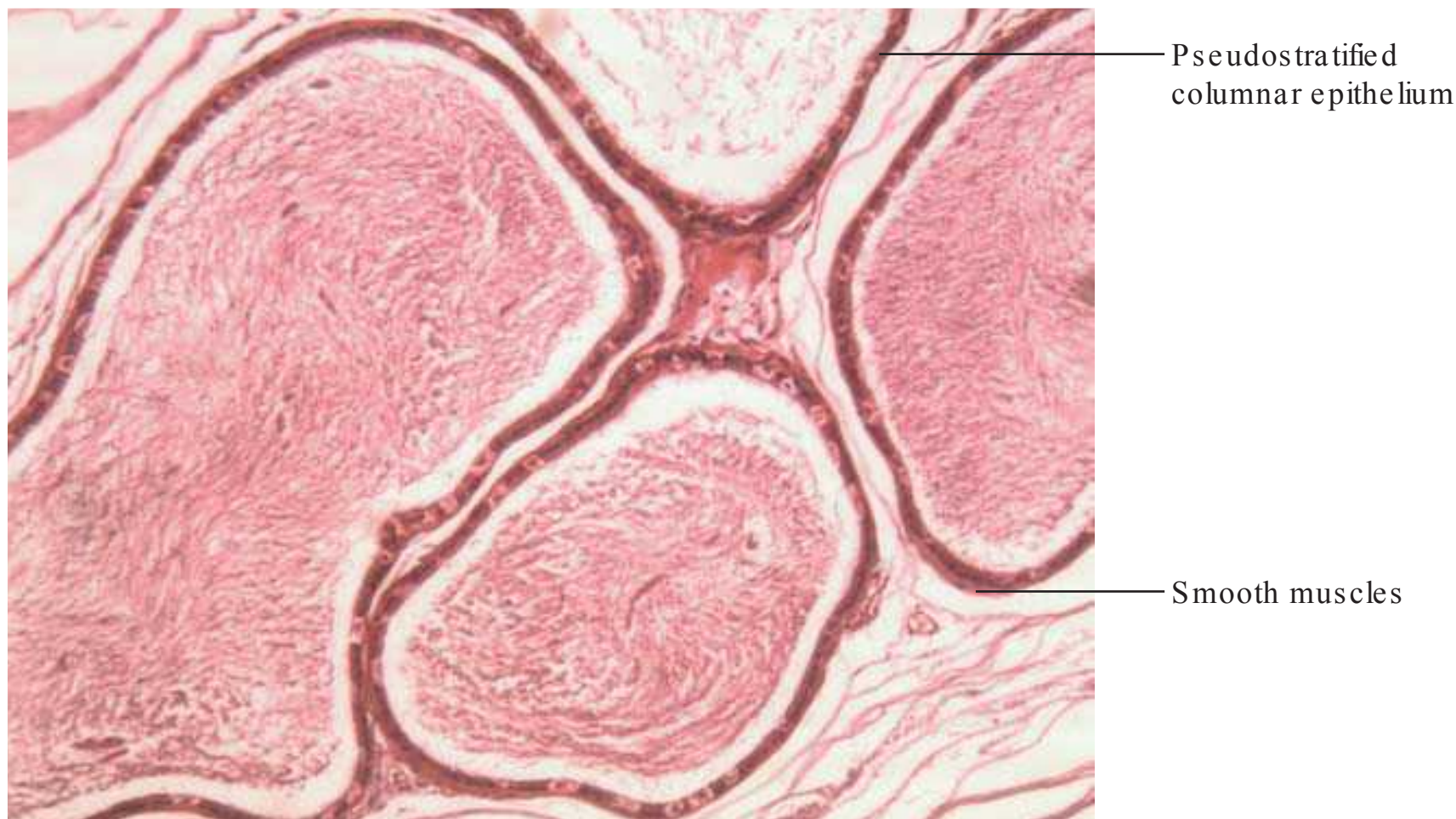
### MICROSCOPIC FEATURES (Fig. 17.8; PMG 17.2)

- Epididymis is lined by pseudostratified columnar epithelium which rests on a basement membrane. (It should be noted that the epithelium of large airways of the respiratory tract is pseudostratified columnar epithelium with goblet cells, whereas the same epithelium in parts of the male reproductive system is devoid of goblet cells.)
- The epithelium has two types of cells: principal cells and basal cells.
- Principal cells are columnar cells; they have stereocilia (long and non-motile microvilli).
- Basal cells are small and round, present near the basal lamina. These cells are precursors of principal cells.
- Underneath the basement membrane there is a thin layer of circularly arranged smooth muscles, which gradually thicken along the length of the duct. In the terminal part of epididymis (just before



**Figure 17.8** Section of epididymis in low magnification. Inset shows an enlarged view of a part of epididymis. (H&E pencil drawing)





**PMG 17.2** Epididymis (H&E stain, X10).

the beginning of vas deferens), the smooth muscles are arranged in three layers: middle circular and inner and outer longitudinal layers. These muscles produce peristaltic contractions which propel the contents towards the vas deferens.

- The duct is surrounded by connective tissue.

## **FUNCTIONS**

- In the epididymis, the spermatozoa are stored and they develop motility during this period. The cells of lining epithelium perform three functions: absorption, phagocytosis and secretion.
- The fluid produced in the seminiferous tubules is absorbed in the proximal part of the epididymis.
- The residual bodies are phagocytosed and digested.
- Glycerophosphocholine, sialic acid and glycoproteins are secreted; these substances probably help in maturation of sperms.

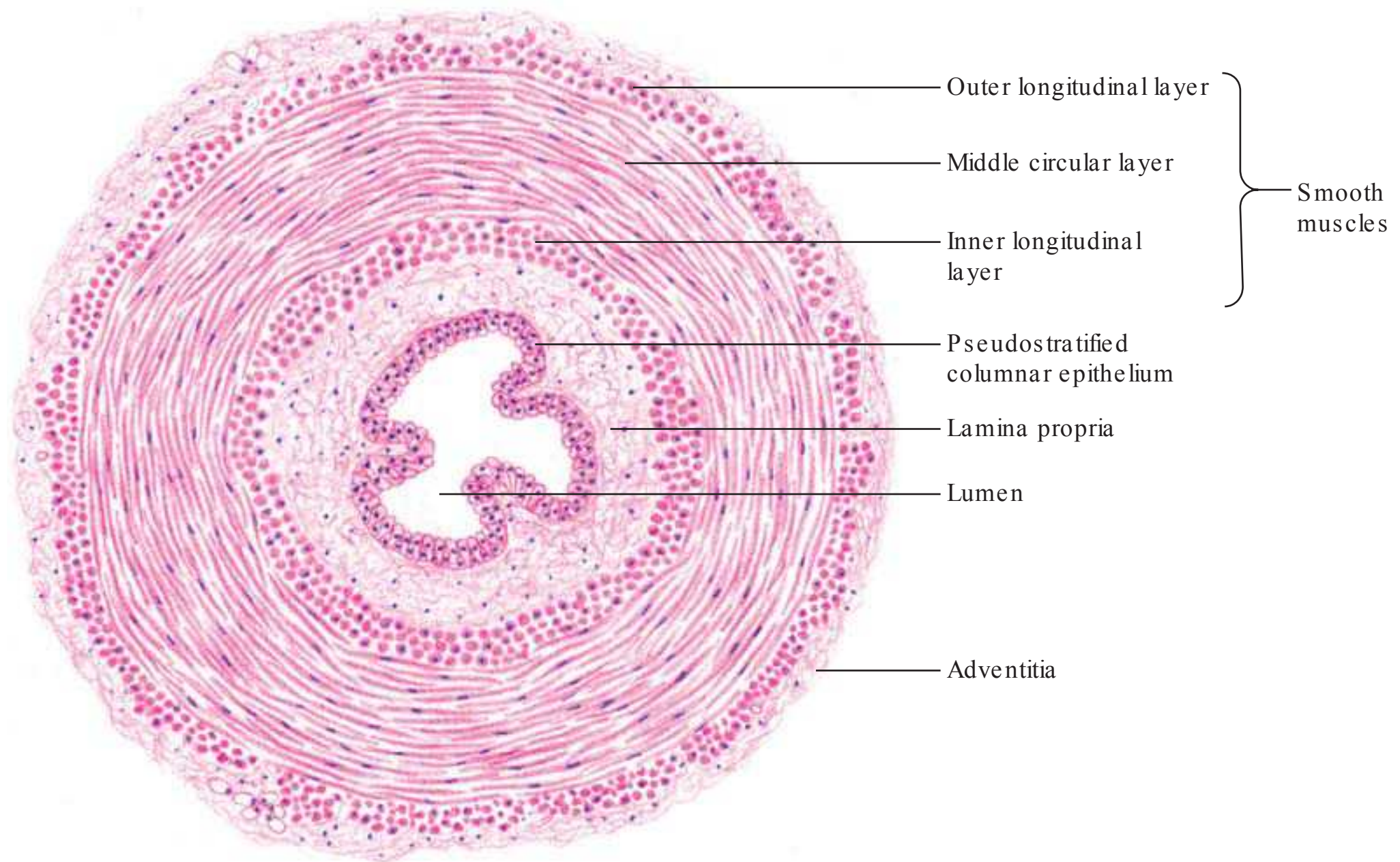
## **VAS DEFERENS**

- The vas deferens is a thick-walled muscular tube which carries the spermatozoa from the epididymis to the ejaculatory duct.
- It begins as a continuation of the epididymis and passes through the inguinal canal as a component of spermatic cord. It enters the pelvis and passes behind the base of the urinary bladder; in this region it dilates to form the ampulla (Fig. 17.1). Finally, it joins the duct of seminal vesicle to form the ejaculatory duct.

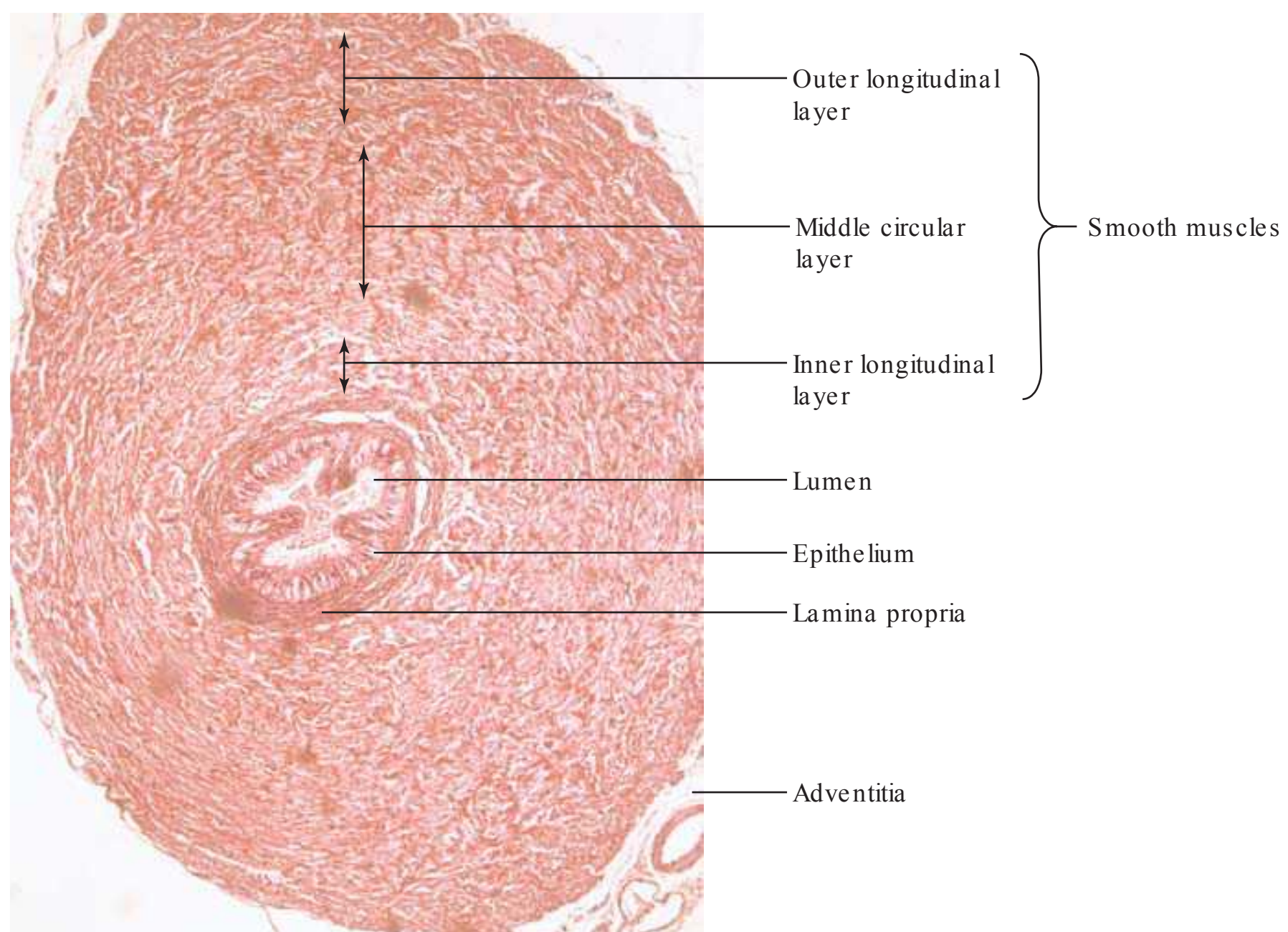
## **MICROSCOPIC FEATURES** (Fig. 17.9; PMG 17.3 and 17.4)

- Mucosa of the vas deferens is folded longitudinally. Similar to the epididymis, it is also lined by pseudostratified columnar epithelium resting on the basement membrane. Epithelial cells have stereocilia.
- The muscular layer is thick and arranged into three layers: inner and outer longitudinal layers and a thick middle layer of circularly arranged smooth muscles. These muscles produce peristaltic contractions during ejaculation.
- Adventitia is present on the outer aspect.





**Figure 17.9** Transverse section of the vas deferens in low magnification (H&E pencil drawing).



**PMG 17.3** Transverse section of the vas deferens (H&E stain, X5).





**PMG 17.4** Transverse section of vas deferens (H&E stain, X10).

## PROSTATE

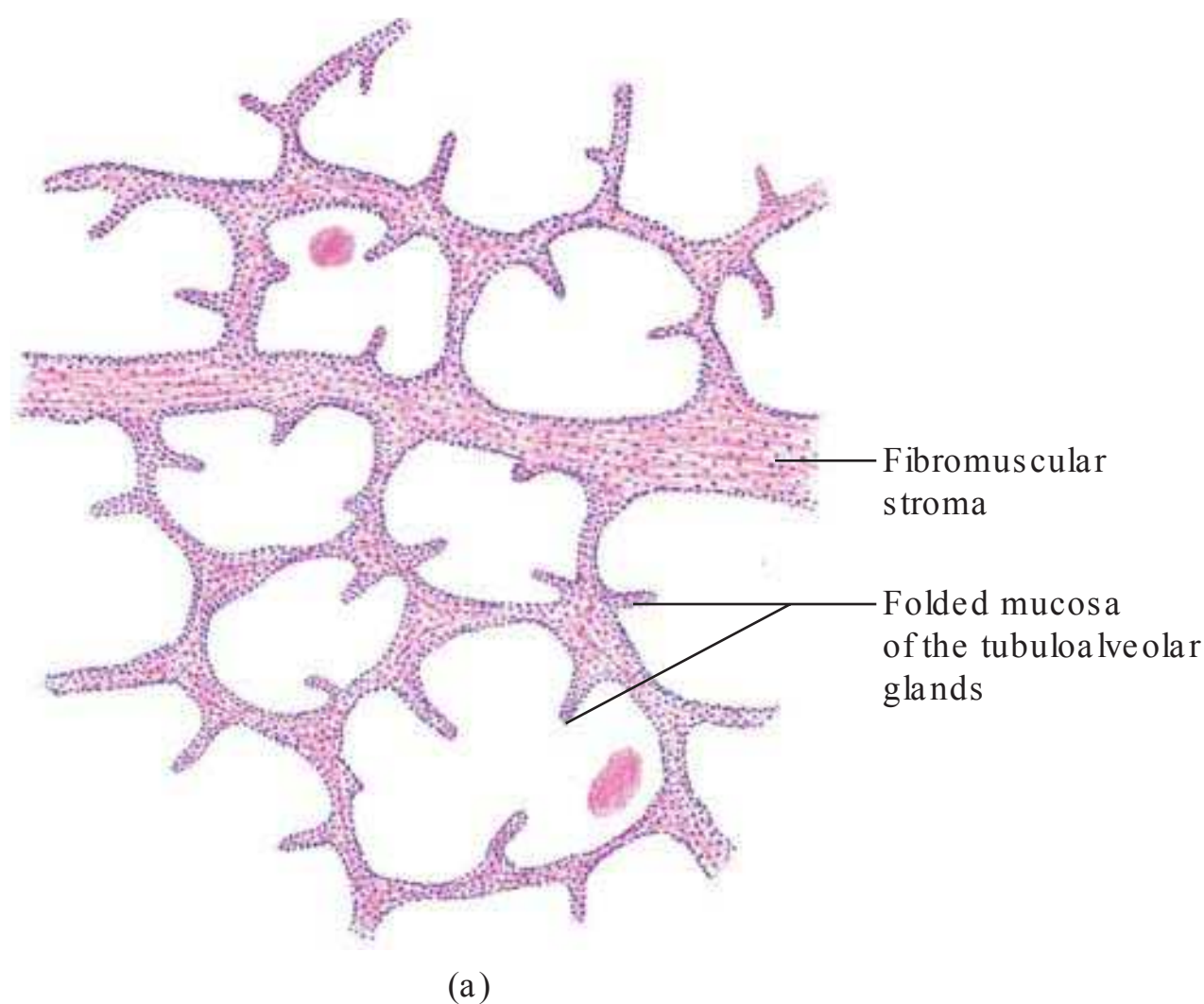
- The prostate is an accessory sex gland in men, present below the neck of the urinary bladder, surrounding the origin of the urethra, in front of the ampulla of rectum (Fig. 17.1).
- Prostatic fluid is a thin milky fluid and constitutes about one-third of the semen volume. It is rich in acid phosphatase. In metastasised prostatic cancer, the concentration of acid phosphatase in the blood increases. Apart from acid phosphatase, prostatic fluid contains fibrinolysin, amylase and citric acid.

### MICROSCOPIC FEATURES (Fig. 17.10; PMG 17.5)

The prostate consists of fibromuscular stroma and parenchyma (tubuloalveolar glands).

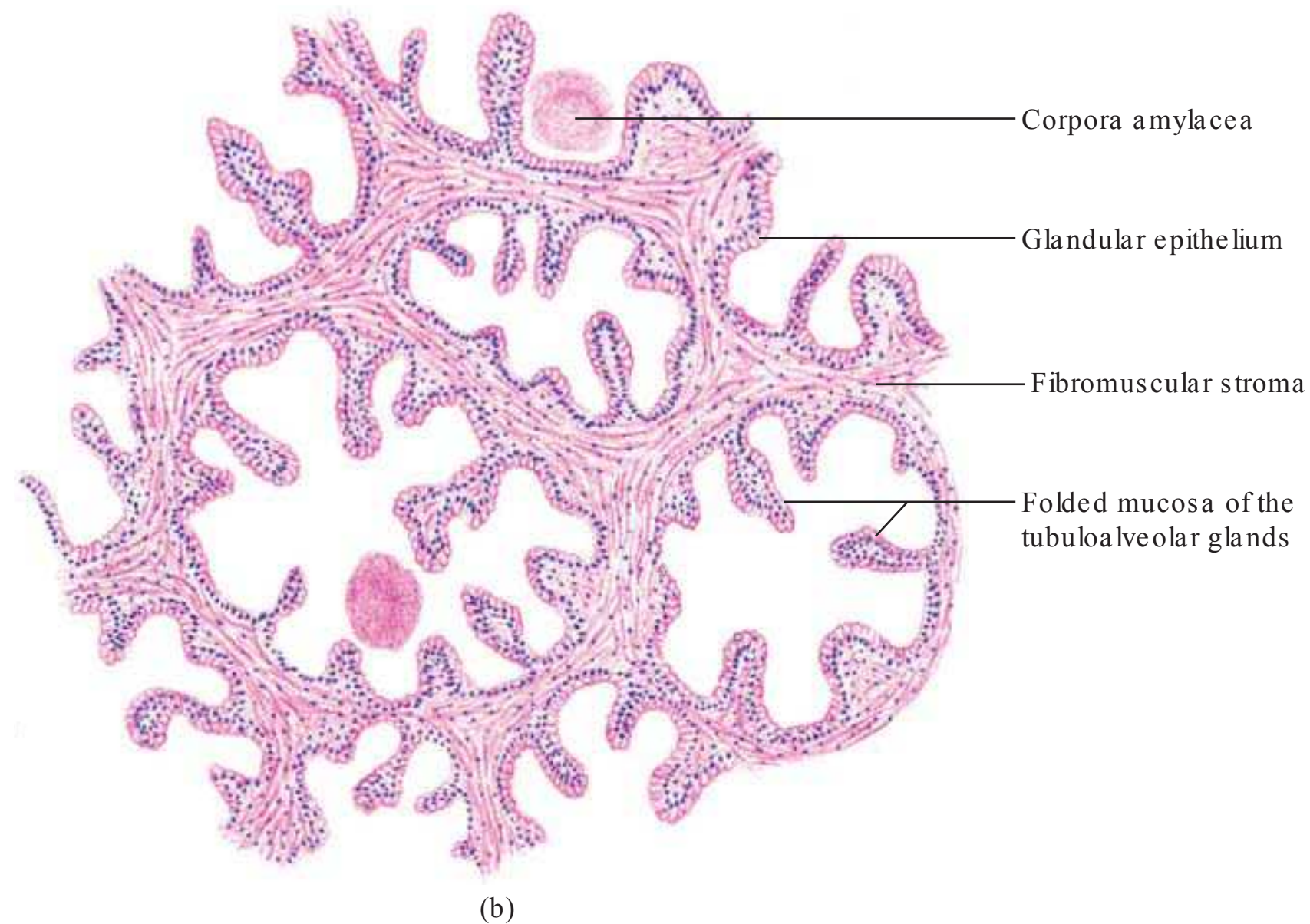
#### Stroma

- The stroma includes a thin capsule that surrounds the entire organ and extensions from the capsule which penetrate the parenchyma.

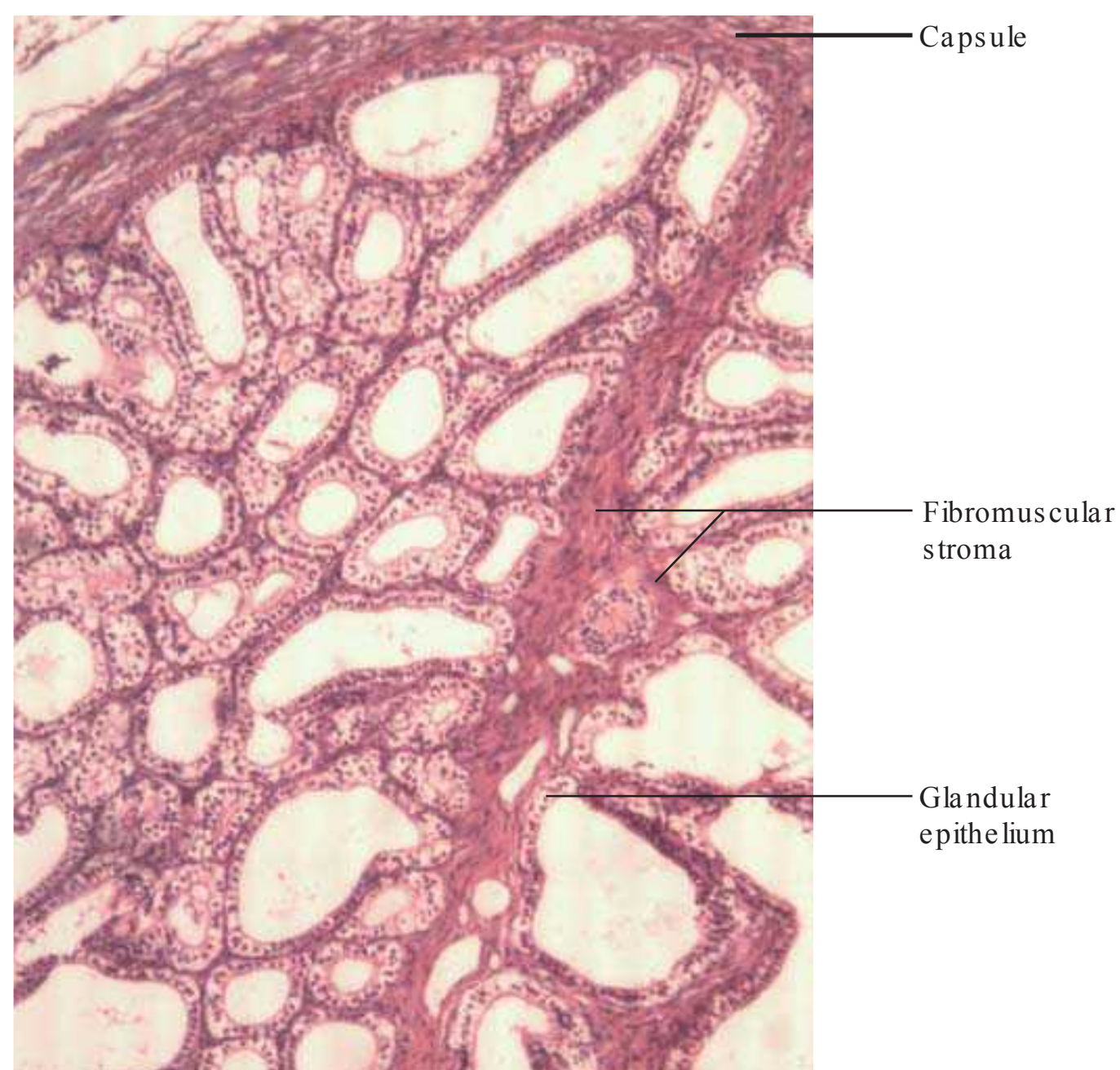


**Figure 17.10** (a) Section of prostate in low magnification (H&E pencil drawing). (continued)





**Figure 17.10** (continued) (b) Section of prostate in high magnification (H&E pencil drawing).



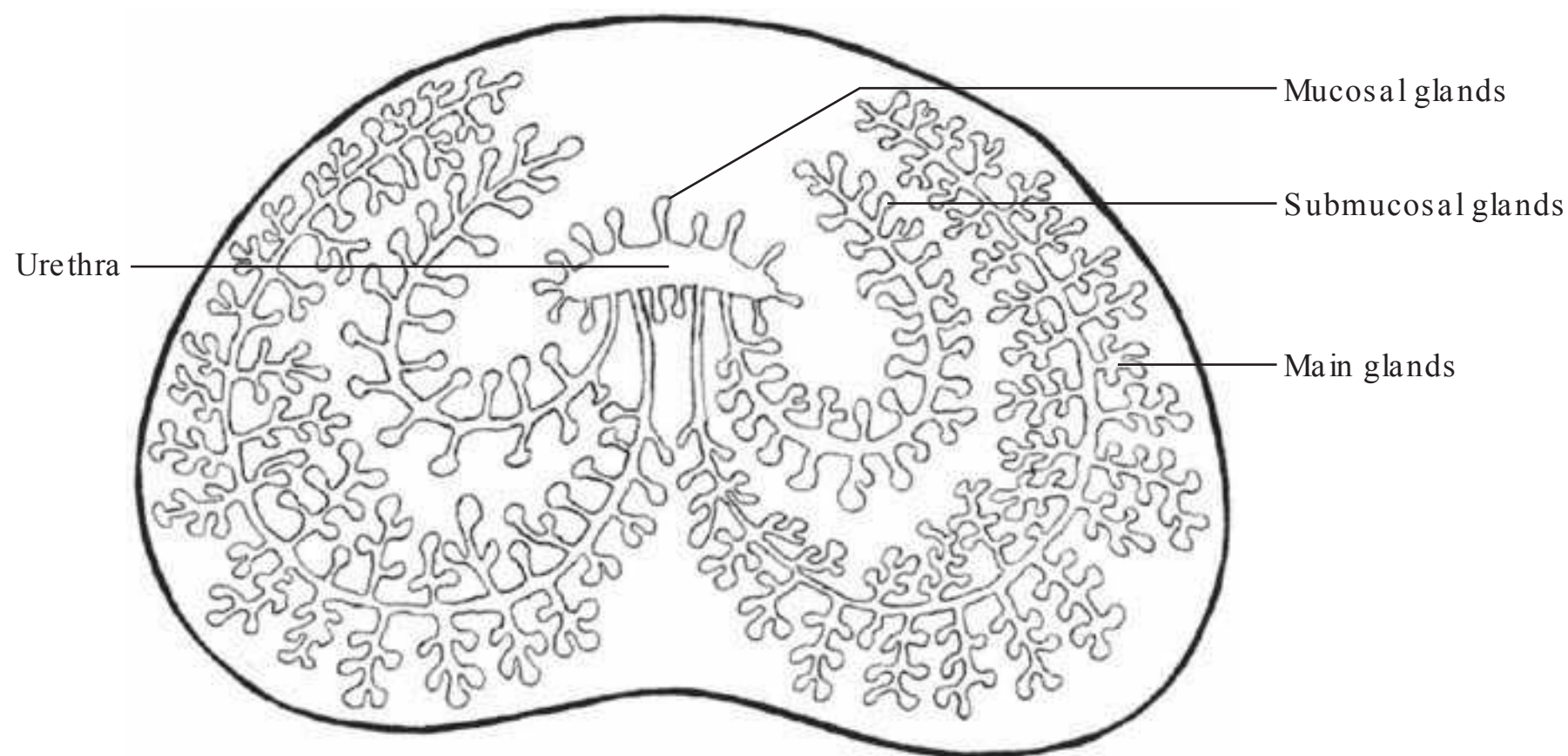
**PMG 17.5** Prostate (H&E stain, X10).

- It consists of fibrous (collagen and elastic fibres) connective tissue and smooth muscles (fibromuscular).
- The smooth muscles present in the stroma contract during ejaculation and propel the secretions of the gland (the prostatic fluid) into the urethra.

### Parenchyma

- The parenchyma consists of 30–50 tubuloalveolar glands.
- These glands are arranged in three concentric layers: inner mucosal, intermediate submucosal and outer main glands (Fig. 17.11).





**Figure 17.11** Transverse section of prostate gland showing the arrangement of various glands.

- The mucosal glands open directly into the urethra; the submucosal and main glands open into the urethra through ducts.
- The mucosa of these glands is highly folded. The epithelium varies with the activity of the glands—in an inactive gland it is simple cuboidal/columnar, and in an active gland it is pseudostratified epithelium (Fig. 17.10b; PMG 17.5).
- Some of the secretory alveoli show rounded eosinophilic bodies called corpora amylacea (Fig. 17.10b). These are secreted substances that with time have become calcified. They are more common in older men.

### Ducts

- As mentioned earlier, the submucosal and main glands open into the urethra through ducts. There are 12–20 independent ducts opening into the urethra (Fig. 17.11).
- The ducts are lined by a simple columnar epithelium which changes to a transitional epithelium in the terminal part.

## SEMINAL VESICLE

The seminal vesicles are a pair of elongated sac-like glands located at the base of the urinary bladder (Fig. 17.1). The secretion from seminal vesicles constitutes around 70% of the total ejaculate. The secretion is yellow, rich in fructose and provides nutrition to the sperms. The secretion is slightly alkaline in nature, and it neutralises the acidic secretion present in vagina, which is essential for survival of sperms.

### MICROSCOPIC FEATURES (Fig. 17.12)

Seminal vesicle consists of three layers: mucosa, muscular layer and adventitia.

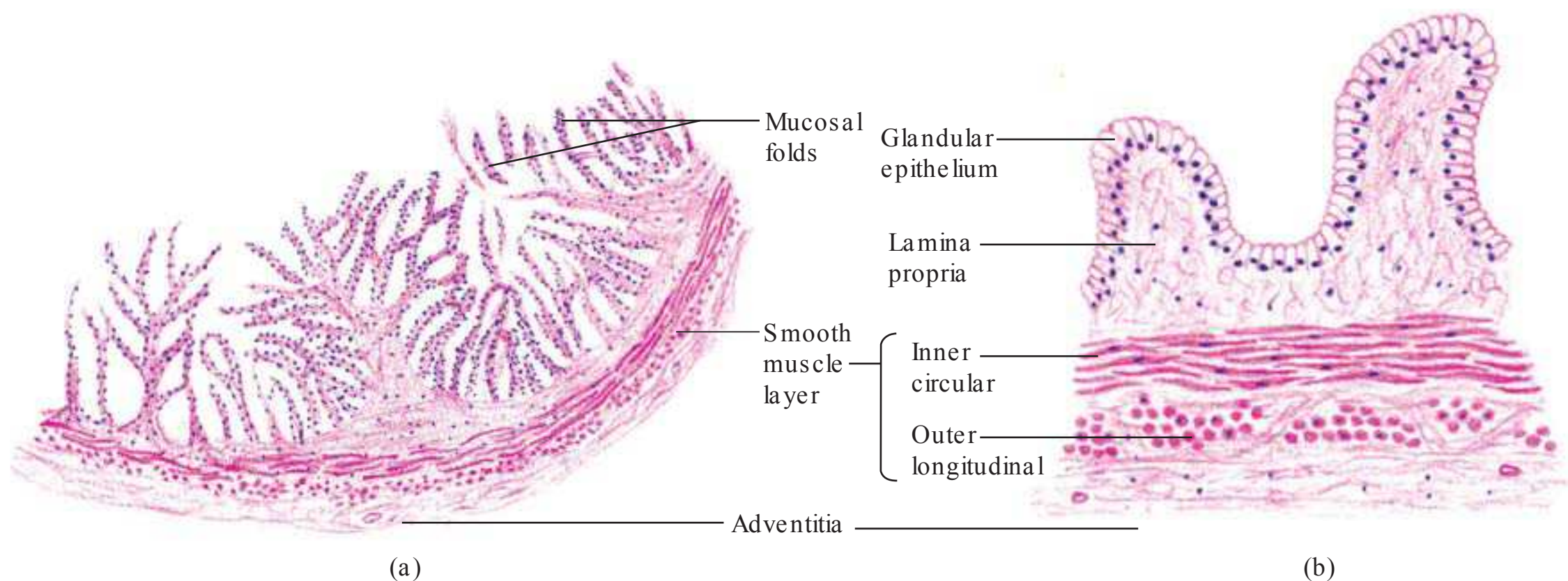
#### Mucosa

- The mucosa is highly folded. It consists of pseudostratified columnar (non-ciliated) epithelium and lamina propria. Lamina propria consists of loose connective tissue.

#### Muscular Layer

- Underlying the lamina propria is the muscular layer, which consists of smooth muscles arranged in inner circular and outer longitudinal layers.





**Figure 17.12** Section of seminal vesicle in (a) low and (b) high magnification (H&E pencil drawing).

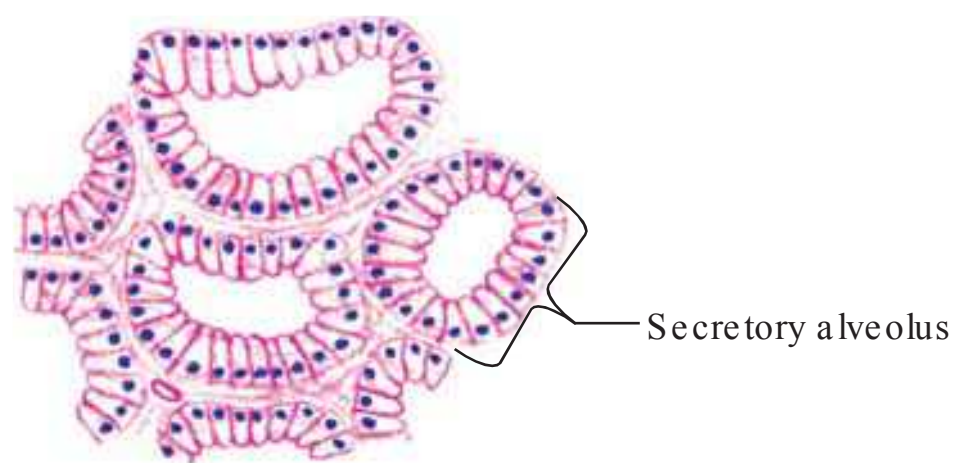
- Contraction of these muscles during ejaculation releases the secretory product into the ejaculatory duct.

#### Adventitia

- This is a layer of connective tissue outside the muscular layer.

### BULBOURETHRAL GLANDS

- Bulbourethral glands are a pair of accessory sex glands in males, located in the urogenital diaphragm (Fig. 17.1).
- These are tubuloalveolar glands lined by simple cuboidal or columnar epithelium (Fig. 17.13). The ducts of the glands open into the penile part of urethra; they are lined by simple columnar epithelium that becomes pseudostratified in the terminal part.
- Each bulbourethral gland is surrounded by a capsule which consists of connective tissue and smooth and skeletal muscles.

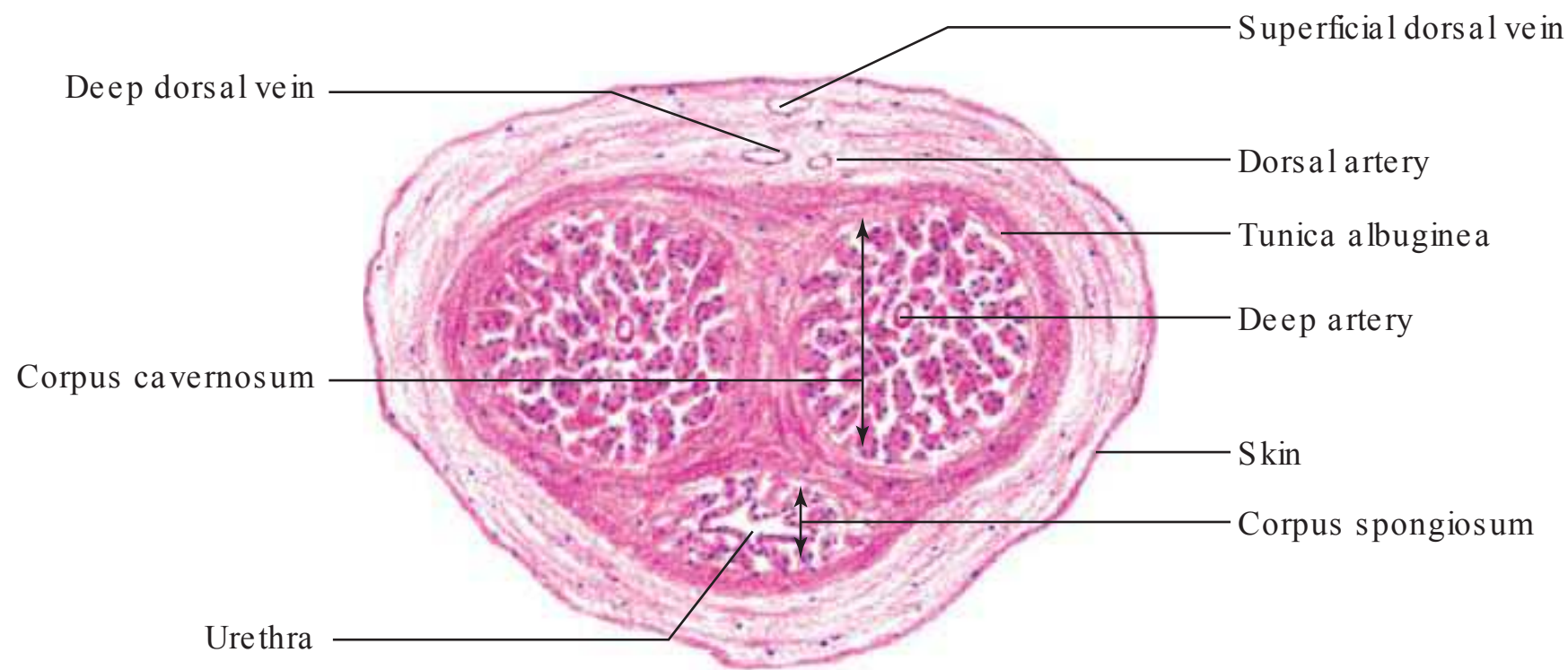


**Figure 17.13** Section of bulbourethral gland in high magnification (H&E pencil drawing).

### PENIS

- Penis consists of three erectile tissues: a pair of dorsally located corpora cavernosa (singular: corpus cavernosum) and a ventrally located corpus spongiosum which surrounds the penile urethra. The terminal part of the corpus spongiosum expands to form glans penis.
- The erectile tissue consists of irregular vascular spaces lined by endothelium.
- These vascular spaces are separated from each other by interconnecting trabeculae (Fig. 17.14) which consist of fibroelastic connective tissue and smooth muscles. Filling of these vascular spaces causes erection of the penis.





**Figure 17.14** Section of penis in low magnification (H&E pencil drawing).

- The three erectile tissues are surrounded by thick fibrous connective tissue called tunica albuginea (Fig. 17.14).
- Surrounding the tunica albuginea, there is a layer of very loose elastic connective tissue and hairless skin.

## CLINICAL CORRELATES

### Male Infertility

- It can be due to hormonal imbalance (Cushing's syndrome, hyperprolactinaemia, isolated FSH deficiency, etc.), testicular causes (Klinefelter's syndrome, gonadotoxins [drugs, radiation], orchitis, trauma, etc.) or disorders of sperm transport (obstruction of epididymis or vas deferens).

### Kartagener's Syndrome

- This is also called immotile cilia syndrome. In this condition, the cilia of the epithelial cells and sperms are defective; as a result the sperm becomes immotile and cannot fertilise. Kartagener's syndrome is also associated with bronchiectasis and chronic sinusitis.

### Benign Prostatic Hyperplasia

- It is a fairly common disease affecting men over the age of 50 years. The enlargement is due to proliferation of glandular tissue or fibromuscular stroma.

### Adenocarcinoma

- Prostate is prone to malignant neoplasm. Malignant transformation is associated with an elevated level of prostate-specific antigen (PSA) in the blood.

## KEYPOINTS

### Testis

The testis is divided into around 250 lobules by numerous septa from mediastinum testis.

### Components of Lobules (Fig. 17.4; PMG 17.1)

#### 1. Seminiferous tubules

- Each lobule of the testis contains one to four seminiferous tubules. Adjacent seminiferous tubules join to form a network of tubules called rete testis from which efferent ductules arise and enter the head of epididymis.

- The seminiferous tubules are lined with stratified seminiferous epithelium which consists of cells in different stages of spermatogenesis and Sertoli cells.
- Sertoli cells are pyramid-shaped cells with ovoid nuclei.

## 2. Leydig cells

- They are present in clusters, in between the seminiferous tubules.
- These are polygonal cells with round nuclei.

## Ducts

Ducts	Lining epithelium	Muscular layer	Functions
Epididymis (Fig. 17.8; PMG 17.2)	<ul style="list-style-type: none"> <li>• Pseudostratified columnar epithelium having principal cells and basal cells</li> <li>• Principal cells have stereocilia</li> </ul>	<ul style="list-style-type: none"> <li>• Circularly arranged smooth muscles</li> <li>• In the terminal part, the arrangement of smooth muscles is similar to vas deferens</li> </ul>	Absorption, phagocytosis and secretion
Vas deferens (Fig. 17.9; PMG 17.4)	<ul style="list-style-type: none"> <li>• Pseudostratified columnar epithelium</li> <li>• Epithelial cells have stereocilia</li> </ul>	<ul style="list-style-type: none"> <li>• The muscular layer is thick</li> <li>• It is arranged into three layers: inner and outer longitudinal layers and a thick middle layer of circularly arranged smooth muscles</li> </ul>	Muscles produce peristaltic contractions during ejaculation

## Prostate (Fig. 17.10; PMG 17.5)

Parts	Features
Fibromuscular stroma	<ul style="list-style-type: none"> <li>• Consists of fibrous connective tissue and smooth muscles</li> </ul>
Parenchyma	<ul style="list-style-type: none"> <li>• 30–50 tubuloalveolar glands</li> <li>• The epithelium varies from simple cuboidal/columnar to pseudostratified epithelium</li> </ul>
Ducts	<ul style="list-style-type: none"> <li>• Ducts are lined by a simple columnar epithelium (Fig. 17.11)</li> </ul>

## Seminal Vesicle (Fig. 17.12)

Layers	Features
Mucosa	Pseudostratified columnar epithelium
Muscular layer	Inner circular and outer longitudinal layers of smooth muscles
Adventitia	A layer of connective tissue

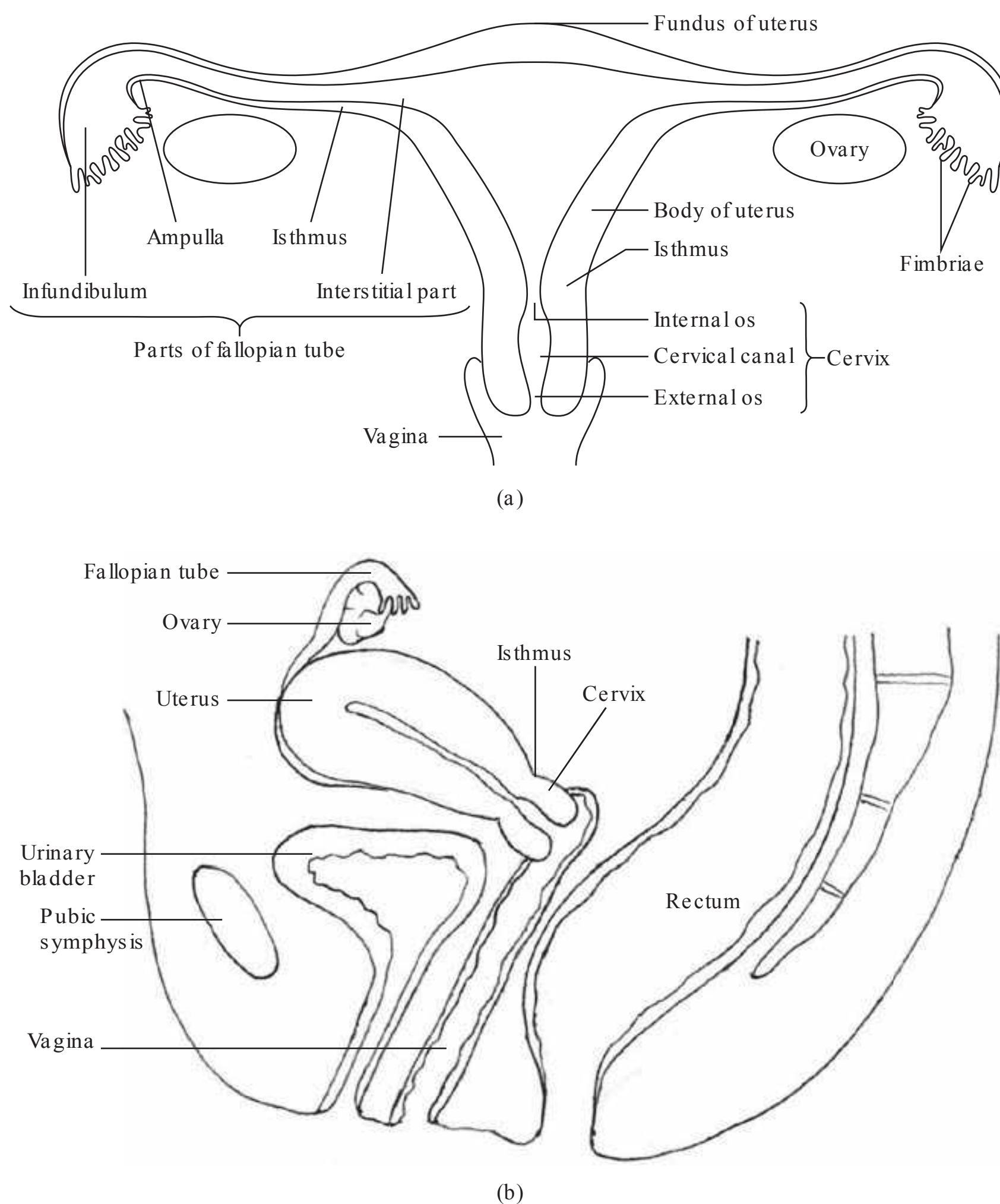
## SELF-ASSESSMENT

1. What do you understand by a lobule of testis? Name its components.
2. Where are the Sertoli cells located in the testis? List their functions.
3. Where are the Leydig cells located in the testis? What do they secrete?
4. List the different stages of spermatogenesis and briefly discuss them.
5. Mention the ducts through which the spermatozoa pass. Which is the lining epithelium of these ducts?
6. Which is the lining epithelium of the glands in the prostate?
7. What is corpora amylacea?



# Female Reproductive System

The female reproductive system consists of ovaries, uterine tubes, uterus, vagina and external genitalia (Fig. 18.1).



**Figure 18.1** The female internal genitalia: (a) front view and (b) lateral view.

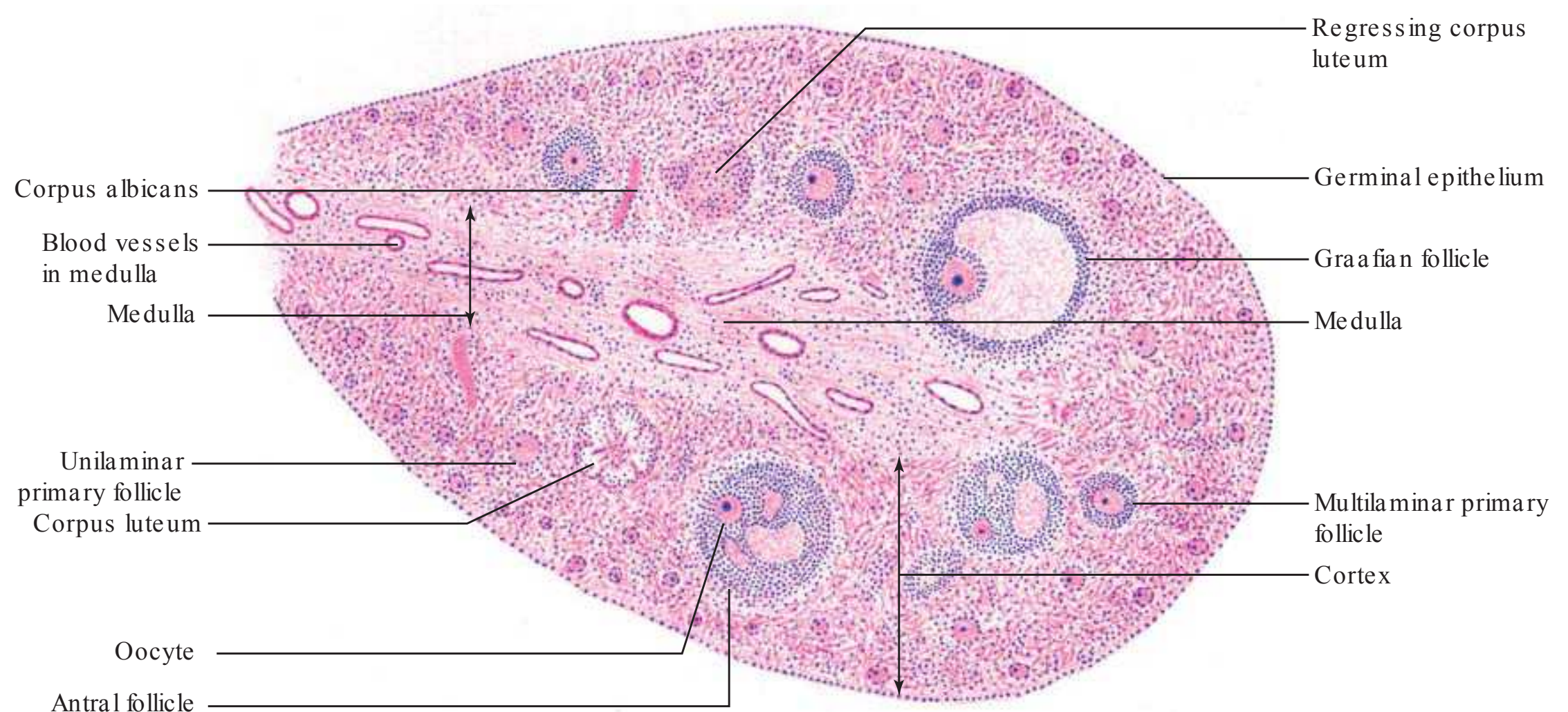


## OVARIES

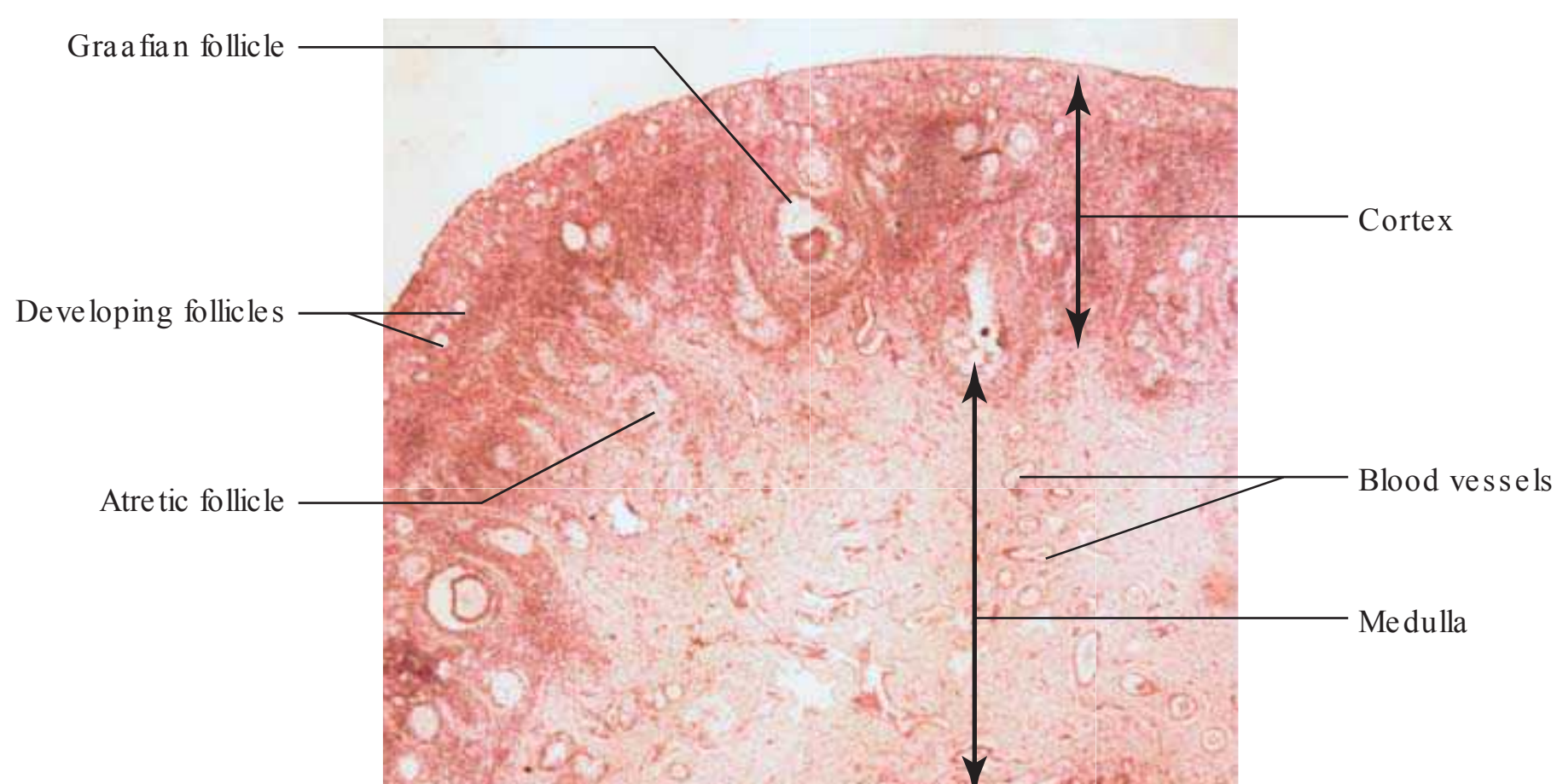
- The ovary is attached to the broad ligament of the uterus by a short fold of peritoneum called the mesovarium. The blood vessels and nerves pass through the mesovarium and enter the ovary.
- Functions: Functions of the ovaries are production and ovulation of oocytes and synthesis and secretion of ovarian hormones (oestrogen and progesterone).

### STRUCTURAL ORGANISATION

- Each ovary consists of two parts: cortex and medulla. Each ovary is covered by germinal epithelium. (Fig. 18.2; PMG 18.1).
- Cortex is the peripheral part of the ovary underneath the coverings. It surrounds the medulla present in the centre.



**Figure 18.2** Section of ovary in low magnification. Parts of the ovary—medulla is in the centre, surrounding the medulla is the cortex and covering the cortex is the germinal epithelium (H&E pencil drawing).



**PMG 18.1** Ovary (H&E stain, X2.5).



- The ovary is covered by simple cuboidal epithelium called germinal epithelium (Fig. 18.3). (Although it is called germinal epithelium, it does not have germ cells—the primordial germ cells migrate from the yolk sac to the ovary.)
- Underneath the germinal epithelium, there is a layer of dense connective tissue called tunica albuginea (Fig. 18.3), which gives white appearance to the ovary.

### Cortex

- It consists of connective tissue (stroma) and ovarian follicles in various stages of development (Fig. 18.2; PMG 18.1).
- Cells of connective tissue (fibroblasts) and fibres run in various directions.

### Medulla

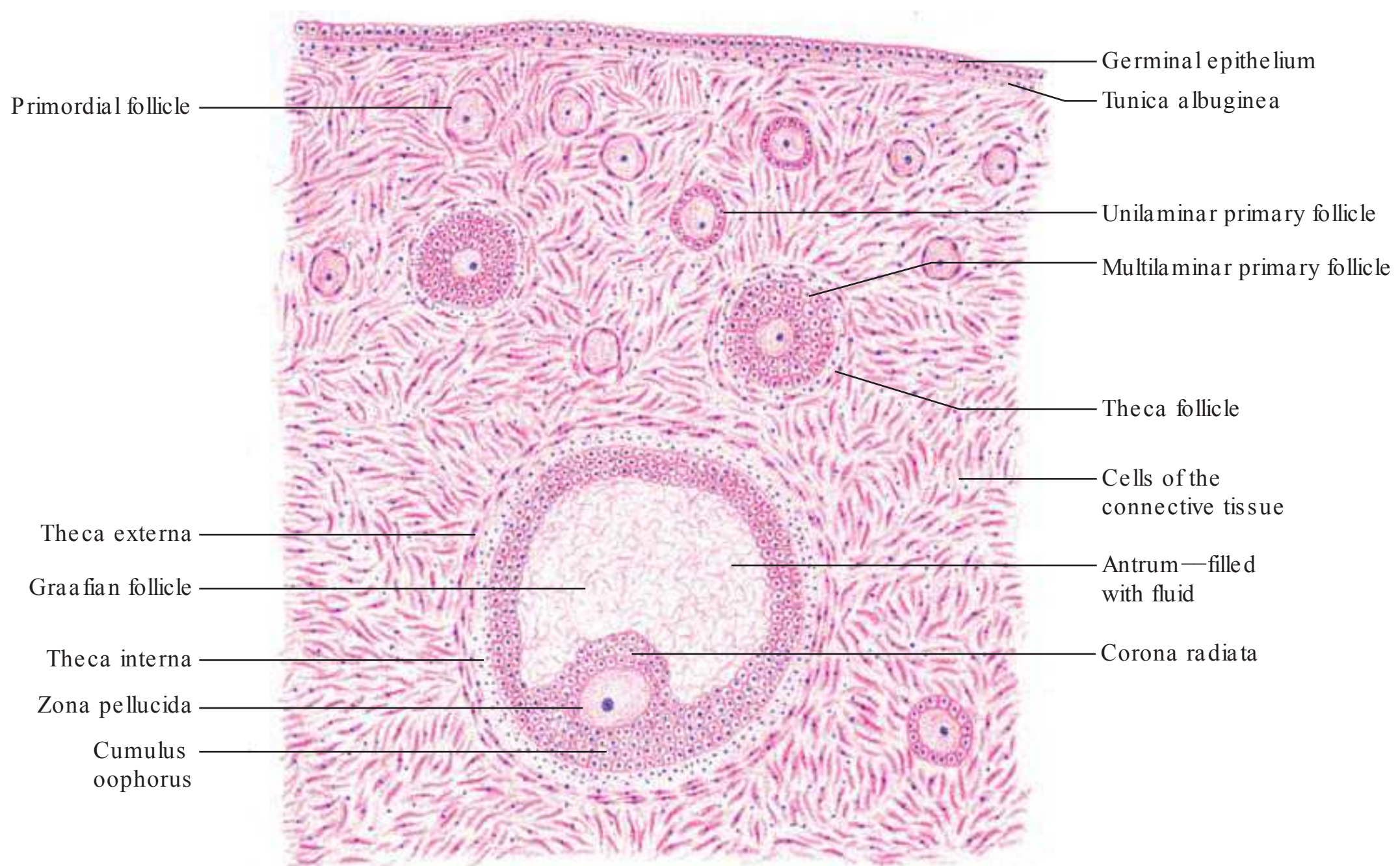
- It consists of connective tissue which is highly vascular (Fig. 18.2; PMG 18.1).

### OVARIAN FOLLICLE

It consists of an oocyte surrounded by follicular cells (also called granulosa cells). Different types of follicles are listed below.

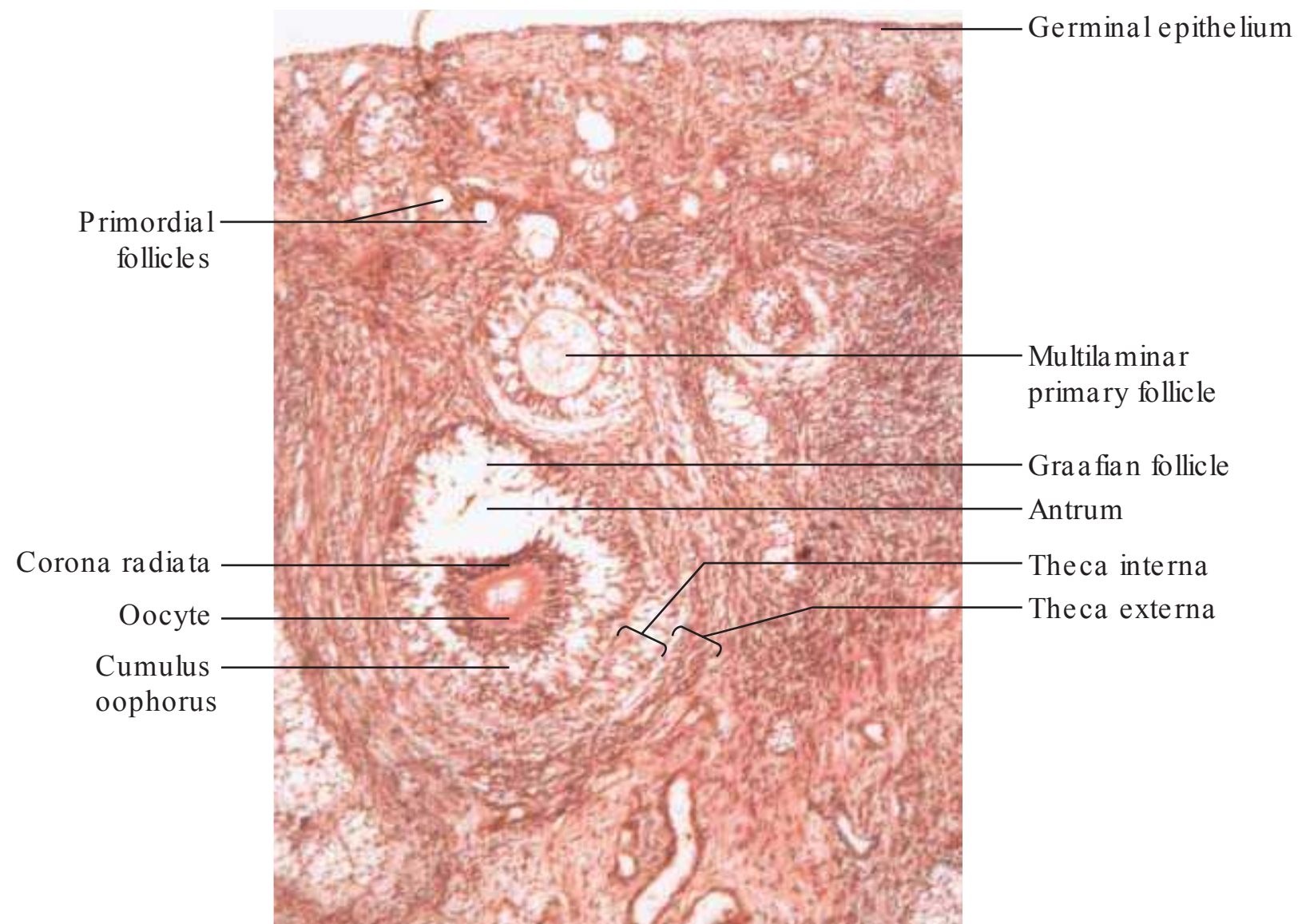
#### Primordial Follicle (Fig. 18.3; PMG 18.2 and 18.3)

- It has an ovum (primary oocyte) which enters the first meiotic division and gets arrested in prophase of meiosis I.
- The ovum is surrounded by a single layer of flat follicular cells.

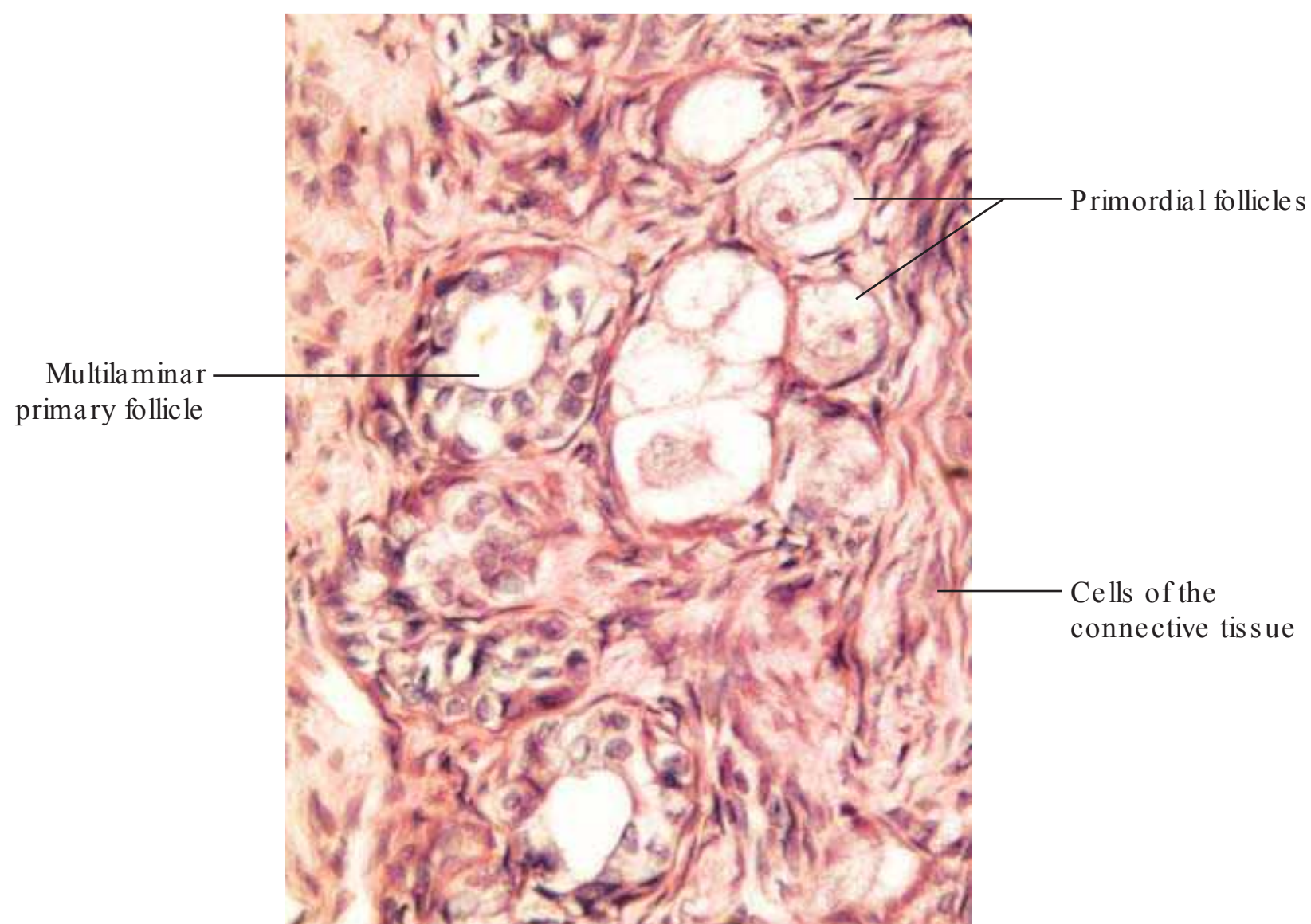


**Figure 18.3** Section of ovary in high magnification. The follicles in various stages of development can be seen. Note the different linings of the primordial follicle (H&E pencil drawing).





**PMG 18.2** Cortex of the ovary showing different types of ovarian follicles (H&E stain, X10).



**PMG 18.3** Cortex of the ovary showing primordial and primary follicles (H&E stain, X40).

- By the seventh month of intrauterine life, all the oogonia are transformed into primary oocytes. The oocyte remains in this stage till puberty, and further development takes place after puberty under the influence of gonadotropins (FSH and LH) secreted by the anterior pituitary.

#### Primary Follicle (Fig. 18.3; PMG 18.2 and 18.3)

- The flat follicular cells become cuboidal; now the follicle is called unilaminar primary follicle.
- A layer of glycoprotein called zona pellucida begins to develop between the oocyte and follicular cells.
- Follicular cells divide and become multilayered around the oocyte; now the follicle is known as multilaminar primary follicle.



- Cells of connective tissue surrounding the ovarian follicle get differentiated to form a layer known as theca follicle. Theca follicle gets differentiated further into two layers: inner theca interna and outer theca externa. A distinct basement membrane separates the granulosa cells from the theca interna.

### Secondary (or Antral) Follicle (Fig. 18.2)

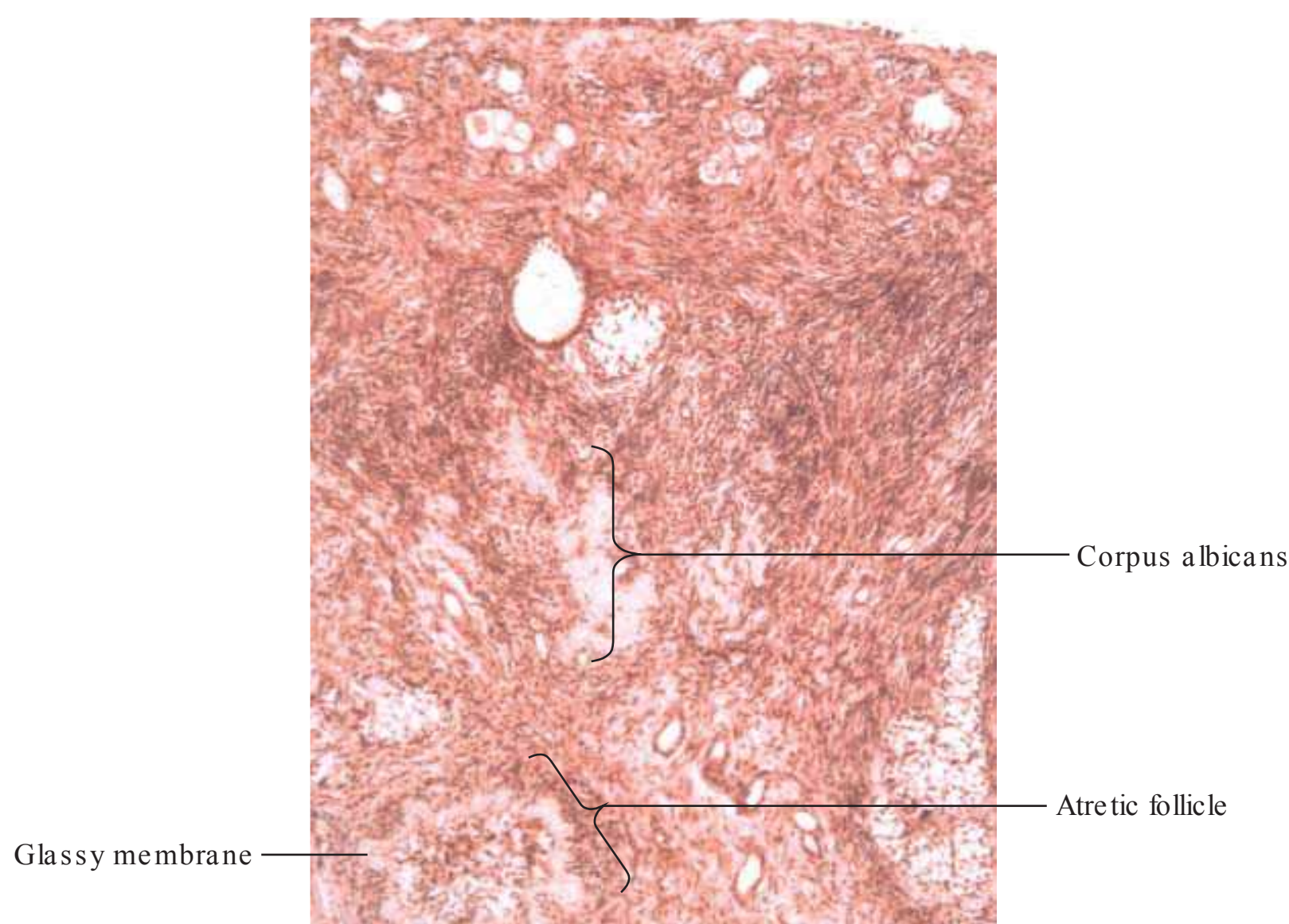
- The follicular cells begin to secrete fluid, called liquor folliculi, which gets accumulated in small cavities in between the follicular cells.
- Theca interna becomes more vascular and begins to secrete oestrogen.

### Graafian Follicle (Figs 18.2 and 18.3; PMG 18.2)

- During each menstrual cycle, one follicle grows more than others and becomes mature (dominant) follicle, called the Graafian follicle, while other developing follicles undergo atrophy.
- The cavities in between the follicular cells coalesce to form a single large antrum.
- The oocyte is displaced to one side of the follicle.
- A few layers of follicular cells that immediately surround the oocyte are called corona radiata.
- Some of the follicular cells concentrate at one point, projecting into the antrum; these cells together are called cumulus oophorus.

### Atretic Follicles

- During each menstrual cycle, one follicle grows more than others and becomes mature follicle, while other developing follicles undergo degeneration which is known as follicular atresia (PMG 18.4).
- Atresia may occur at any stage in the development of a follicle.
- Primordial follicles undergoing atresia are immediately replaced by stroma. Atresia of large follicles leaves collagenous scar, which is gradually replaced by stromal tissue.
- In the atresia of large follicles, follicular cells and oocyte undergo degeneration. Macrophages invade the atretic follicle and phagocytose the degenerating cells. Zona pellucida persists little longer as it resists degenerative changes, but eventually, it is broken down and the remnant is engulfed by macrophages.
- The basement membrane between granulosa cells and the theca interna thickens and becomes wavy, and it is referred to as the glassy membrane (PMG 18.4).



**PMG 18.4** Cortex of the ovary showing atretic follicle (H&E stain, X10).

### During Ovulation

- It occurs on the 14th day of 28-day menstrual cycle.
- Just before the ovulation, the oocyte completes its first meiotic division, giving rise to one secondary oocyte and the first polar body. The secondary oocyte enters the second meiotic division and gets arrested in metaphase until fertilisation takes place. The first polar body lies inside the zona pellucida.
- During ovulation corona radiata containing the secondary oocyte gets detached from cumulus oophorus; the Graafian follicle ruptures and the secondary oocyte with zona pellucida and corona radiata is expelled into the peritoneal cavity.
- If fertilisation occurs, then the second meiotic division is completed, otherwise the ovum undergoes degeneration.

### CORPUS LUTEUM (Fig. 18.2)

- After ovulation, the Graafian follicle forms a temporary endocrine gland called corpus luteum.
- Immediately after ovulation, the wall of the follicle collapses. The capillaries of theca interna bleed and clot is formed in the centre of the follicle. At this stage the follicle is referred to as corpus haemorrhagicum. Later, granulosa cells and theca interna cells undergo changes and corpus luteum is formed.
- Granulosa cells increase in size to form granulosa luteal cells which secrete progesterone.
- Theca interna cells also increase in size to form theca lutein cells which secrete oestrogen.
- If fertilisation does not occur, then corpus luteum is called corpus luteum of menstruation; it degenerates after 14 days.
- If fertilisation occurs, then it is called corpus luteum of pregnancy. It is maintained till the second to third month of pregnancy and after that it degenerates.
- The degeneration of corpus luteum produces a dense connective tissue scar, which is called corpus albicans (Fig. 18.2; PMG 18.4).

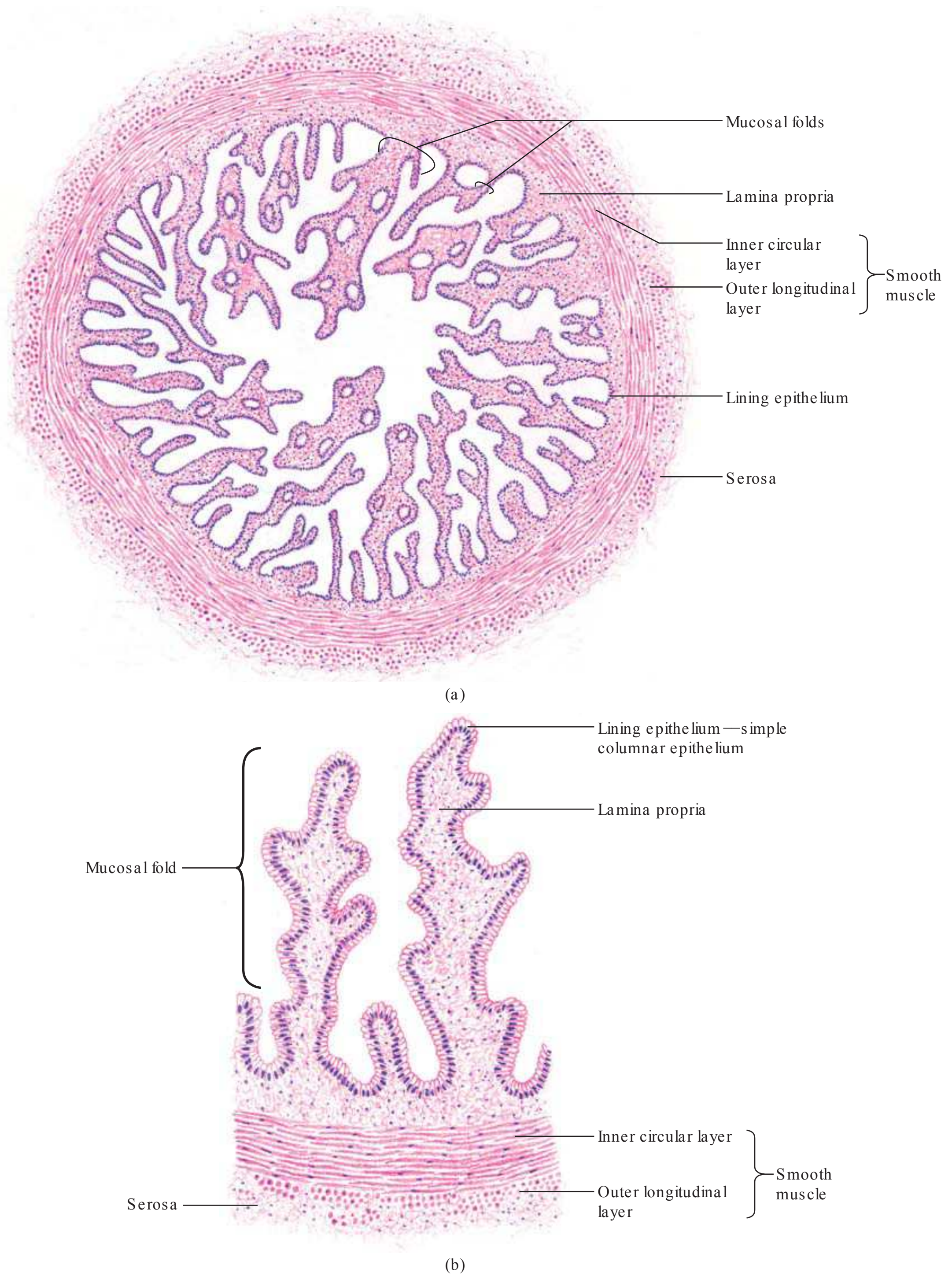
### FALLOPIAN TUBE

- Fallopian tubes are a pair of tubes also called uterine tubes. Each tube communicates with the uterine cavity at its proximal end and with the peritoneal cavity at its distal end which is present near the ovary.
- It has four parts (Fig. 18.1):
  - (a) Interstitial part: This part penetrates the uterine wall and opens into the uterine cavity.
  - (b) Isthmus: This is the narrow part near the uterine wall.
  - (c) Ampulla: This is the dilated middle part.
  - (d) Infundibulum: It is the most distal part; its distal end opens into the peritoneal cavity. It has finger-like projections, the fimbriae.
- The fallopian tube collects the ovum after ovulation. The sperm also enters the fallopian tube from the uterine cavity and fertilisation occurs. After fertilisation, the zygote is transported into the uterine cavity.

### MICROSCOPIC STRUCTURE

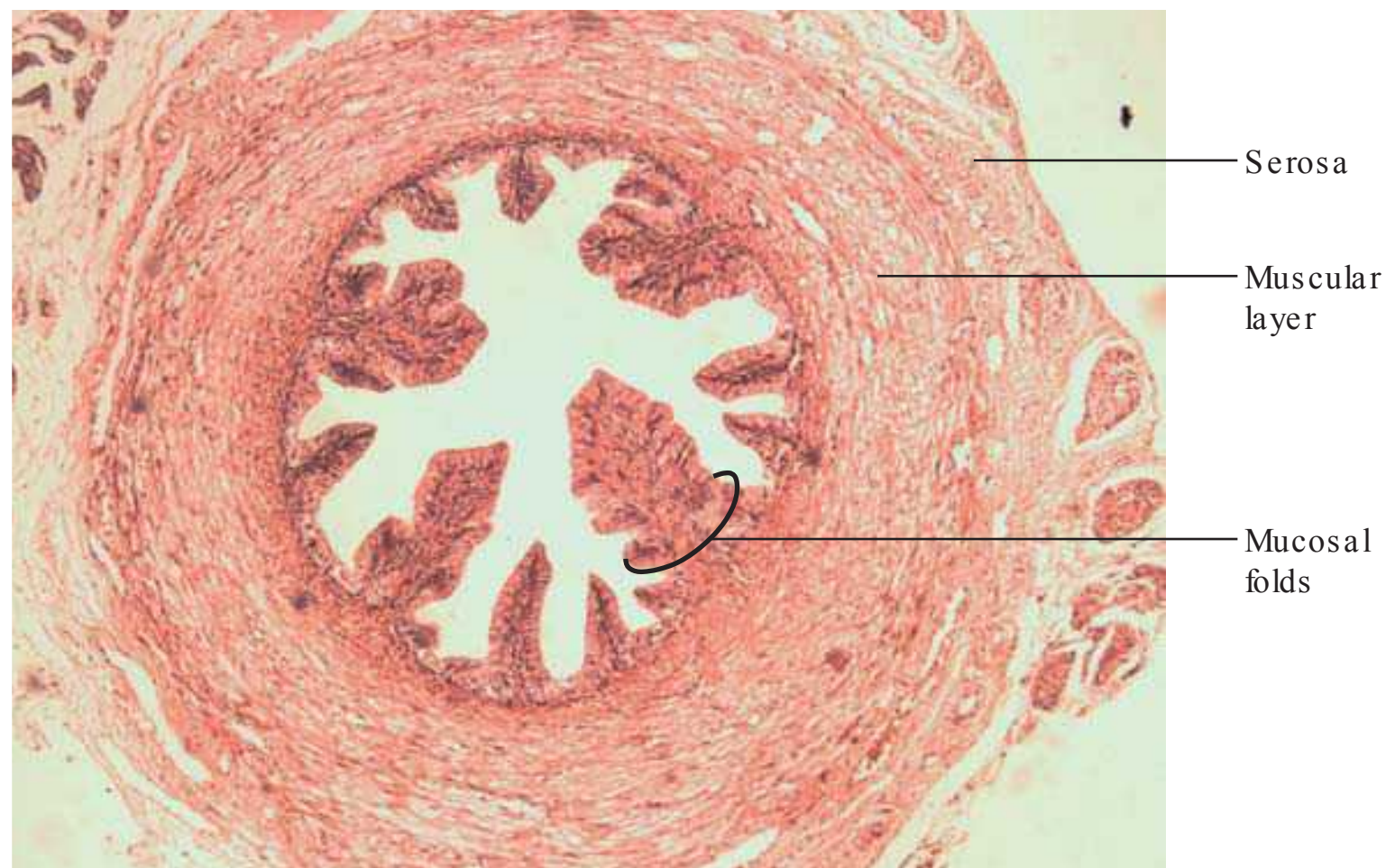
The wall of the fallopian tube has three layers (from lumen to outside): mucosa, muscular layer and serosa (Fig. 18.4; PMG 18.5).





**Figure 18.4** Transverse section of fallopian tube in (a) low and (b) high magnification (H&E pencil drawing).





(a)



(b)

**PMG 18.5** Fallopian tube: (a) X5 and (b) X10 (H&E stain).

### Mucosa

- The mucosa is folded to form numerous longitudinal folds which project into the lumen (Fig. 18.4). Maximum number of these folds are present in the ampulla.
- The mucosa consists of simple columnar epithelium and underlying lamina propria.
- The epithelium has two types of cells: ciliated cells and non-ciliated secretory cells (peg cells). The secretions of peg cells form a thin film over the mucosa; this film along with the fertilised ovum is propelled towards the uterine cavity by the ciliary movements of the ciliated cells. The secretion of the peg cells also provides nutrition to the ovum.

### Muscular Layer

- It lies underneath the mucosa and consists of inner circular and outer longitudinal smooth muscle layers.
- Contractions of these muscles also help in propelling the fertilised ovum.

### Serosa

- It is the outermost layer which consists of a layer of connective tissue and, overlying it, the mesothelium.

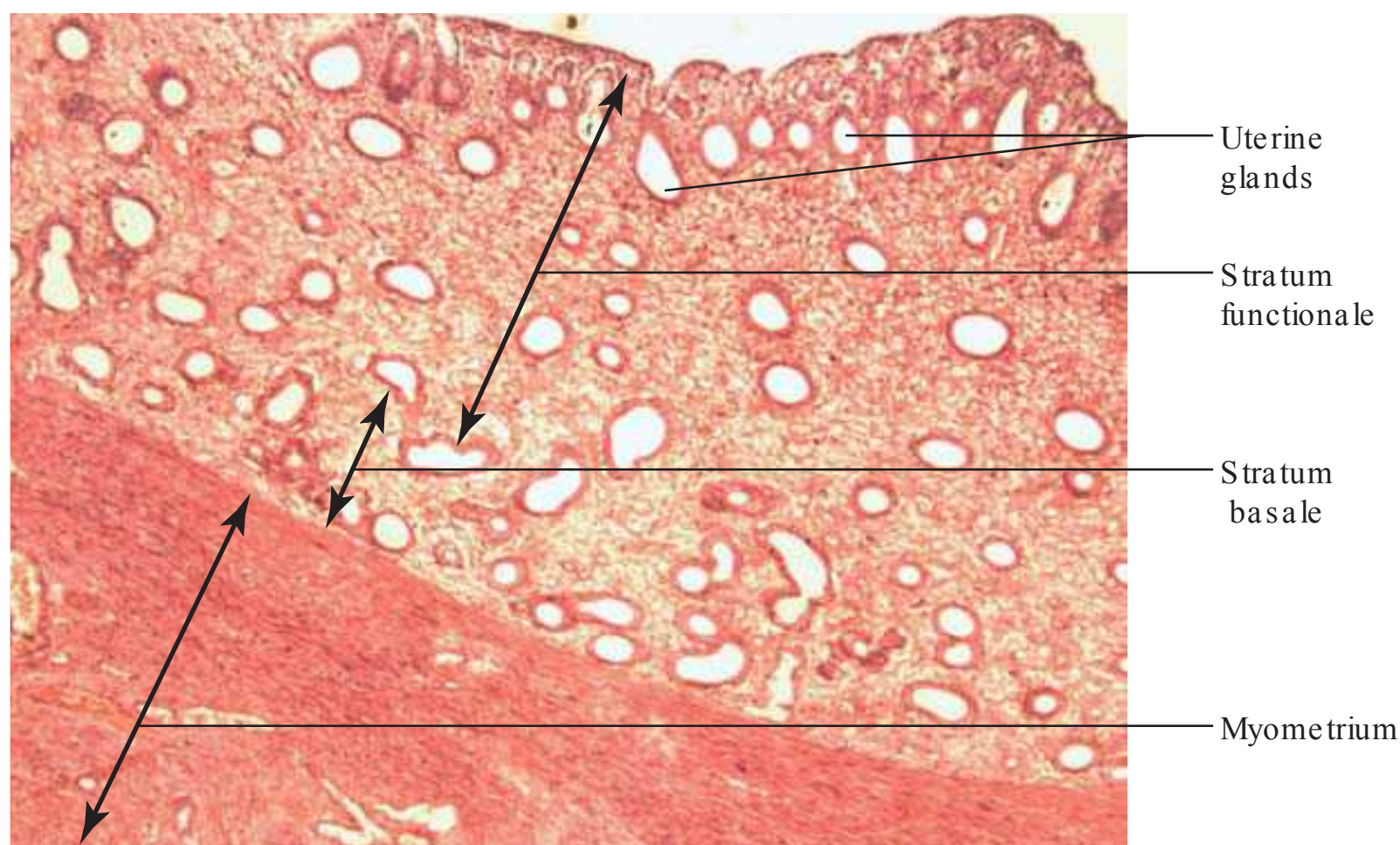


## UTERUS

- The uterus is a pear-shaped organ located in the lesser pelvis between the urinary bladder in front and the rectum behind.
- The cavity of the uterus receives opening of the fallopian tubes on each side and communicates below with the vagina through the cervical canal.
- The uterus consists of three parts: fundus, body and cervix. The fundus is the upper dome-shaped part which is above the attachment of the fallopian tube. The body extends from the fundus to the isthmus; the isthmus is a narrow constricted part separating the body of the uterus from the cervix. Below the isthmus, the uterus becomes cylindrical in shape; this part is known as cervix (Fig. 18.1). The cervix has been discussed separately.
- The uterus is the site for implantation of the zygote.

### MICROSCOPIC STRUCTURE

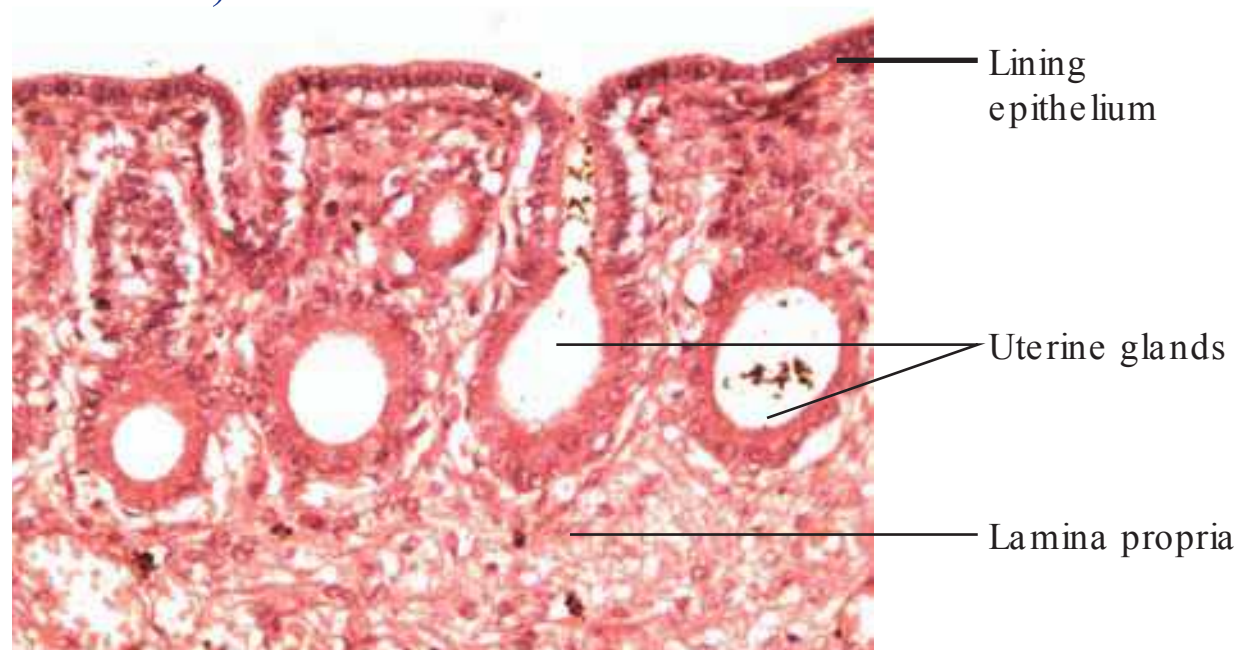
The uterine wall consists of three layers (from inside to outside): endometrium, myometrium and serosa or adventitia (PMG 18.6).



**PMG 18.6** Uterus (H&Estain, X5).

### Endometrium

- Endometrium is the mucosal layer consisting of simple columnar epithelium and underlying lamina propria. Lamina propria has numerous simple tubular glands (endometrial glands) which open on the surface epithelium (PMG 18.7).



**PMG 18.7** Endometrium of the uterus (H&Estain, X20).



- The endometrium undergoes cyclical changes during the menstrual cycle. On the basis of the cyclical changes, it is divided into two layers: stratum functionale and stratum basale. (See Figs 18.6 and 18.7 showing the histology drawings of these layers).
- The stratum functionale is the superficial layer, which constitutes about 80% of the endometrial thickness and is shed during menstruation.
- The stratum basale is the deeper layer, which is not shed during menstruation. The basal part of the endometrial glands is present in this layer.

### Myometrium

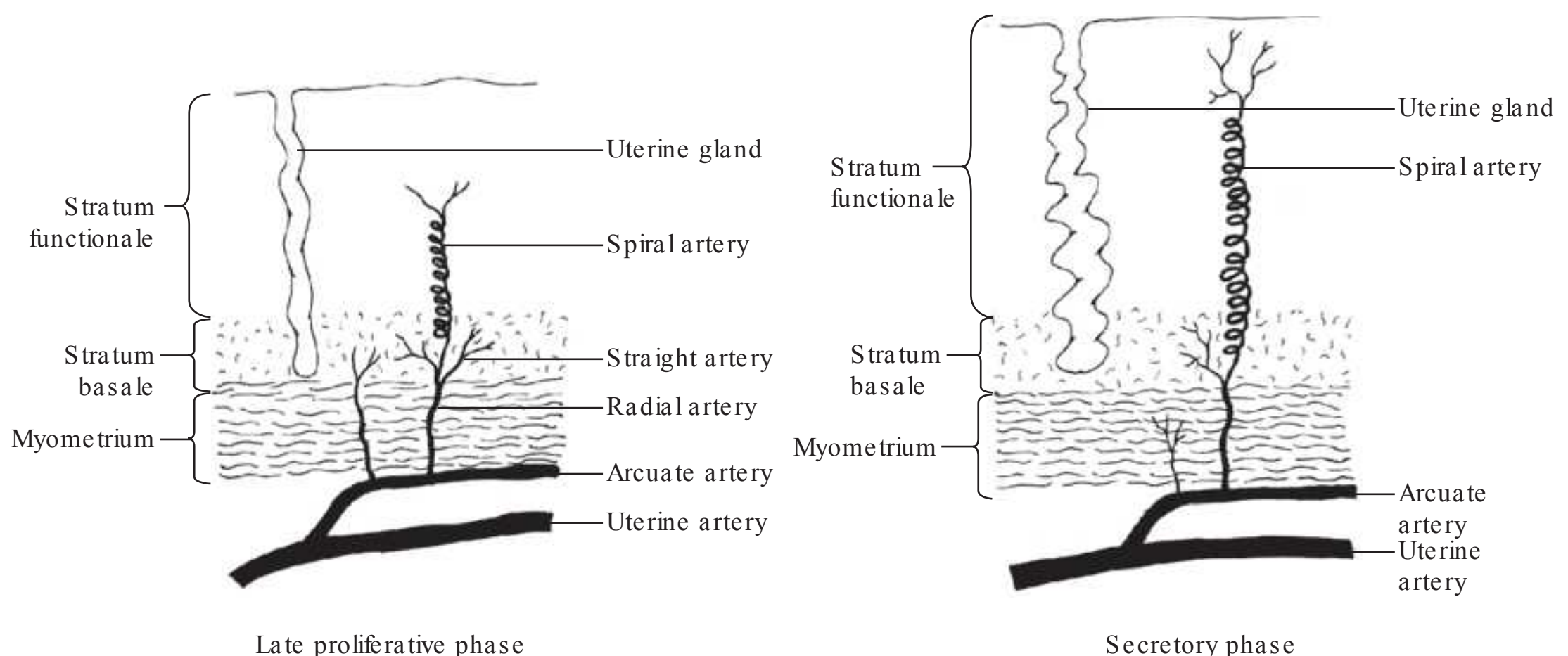
- Underlying the stratum basale there is a muscular layer, the myometrium, which is the thickest layer of the uterine wall (see Figs 18.6 and 18.7).
- Although the smooth muscle bundles are arranged in various directions, the myometrium consists of three ill-defined layers. Out of these, the middle layer is the thickest and also rich in blood supply, and hence this layer is often referred to as stratum vasculare.
- Blood vessels are present in between the smooth muscle bundles.
- The rhythmic contraction of these muscles may intensify during menstruation and cause cramps. During pregnancy, the enlargement of the uterus is primarily due to hypertrophy and hyperplasia of uterine smooth muscles. At parturition, the hormone oxytocin induces powerful contractions of the uterine muscles to expel the foetus.

### Serosa or Adventitia

- It is the outermost layer, also known as perimetrium.
- The part of the uterus covered by peritoneum has serosa, and the remaining part has adventitia.

### BLOOD SUPPLY

- The uterus is supplied by a pair of uterine arteries.
- Each uterine artery gives arcuate branches; arcuate arteries give radial arteries, which supply the myometrium (Fig. 18.5).
- In the myometrium, radial arteries divide into two types of arteries: straight and spiral arteries.
- Straight arteries are in stratum basale and spiral arteries (which are long and coiled) are in the stratum functionale.
- During menstruation, spiral arteries are shed along with the stratum functionale.

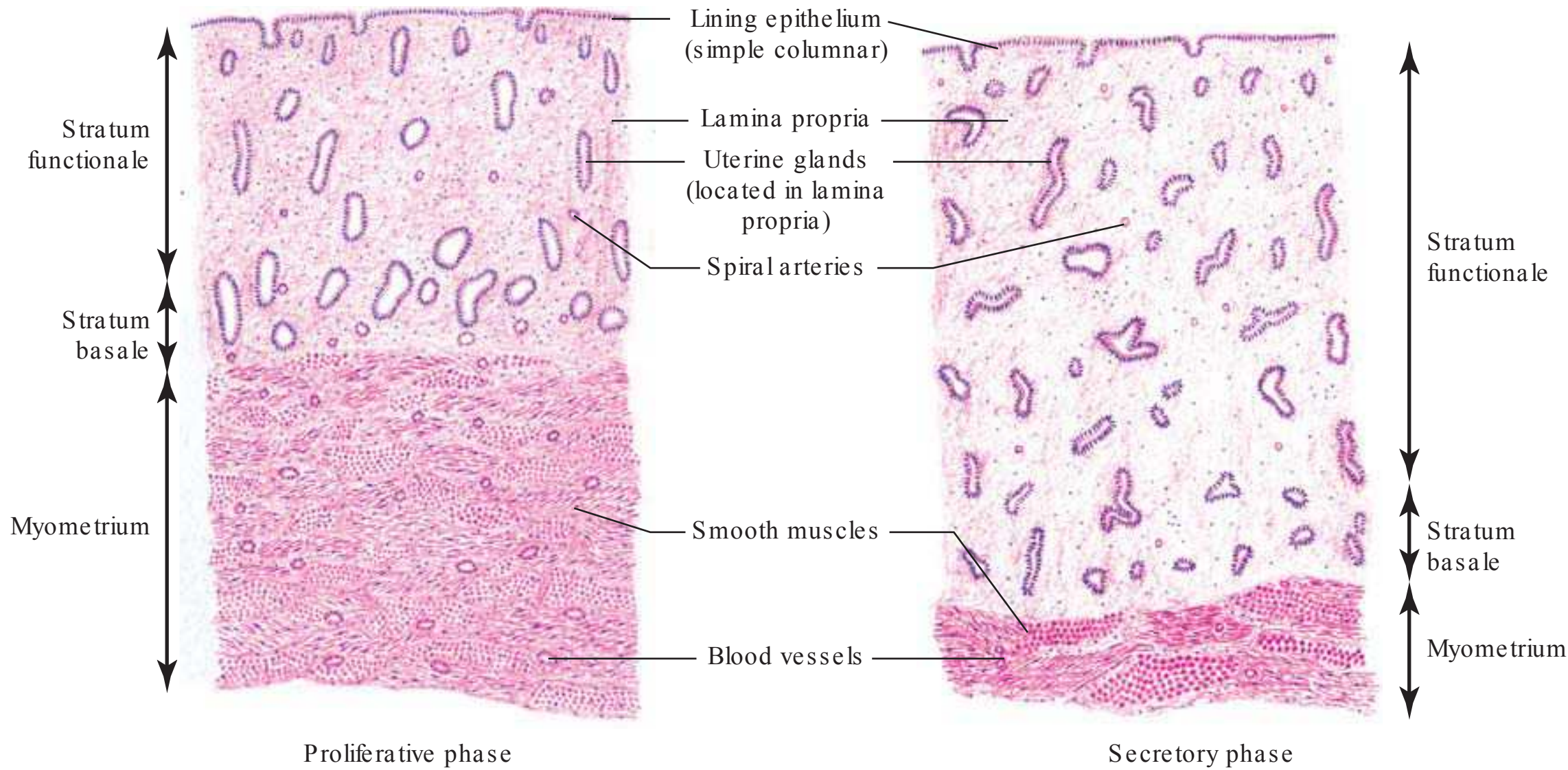


**Figure 18.5** Schematic diagram showing two layers of uterine endometrium, stratum functionale and stratum basale, and its blood supply in proliferative and secretory phases.

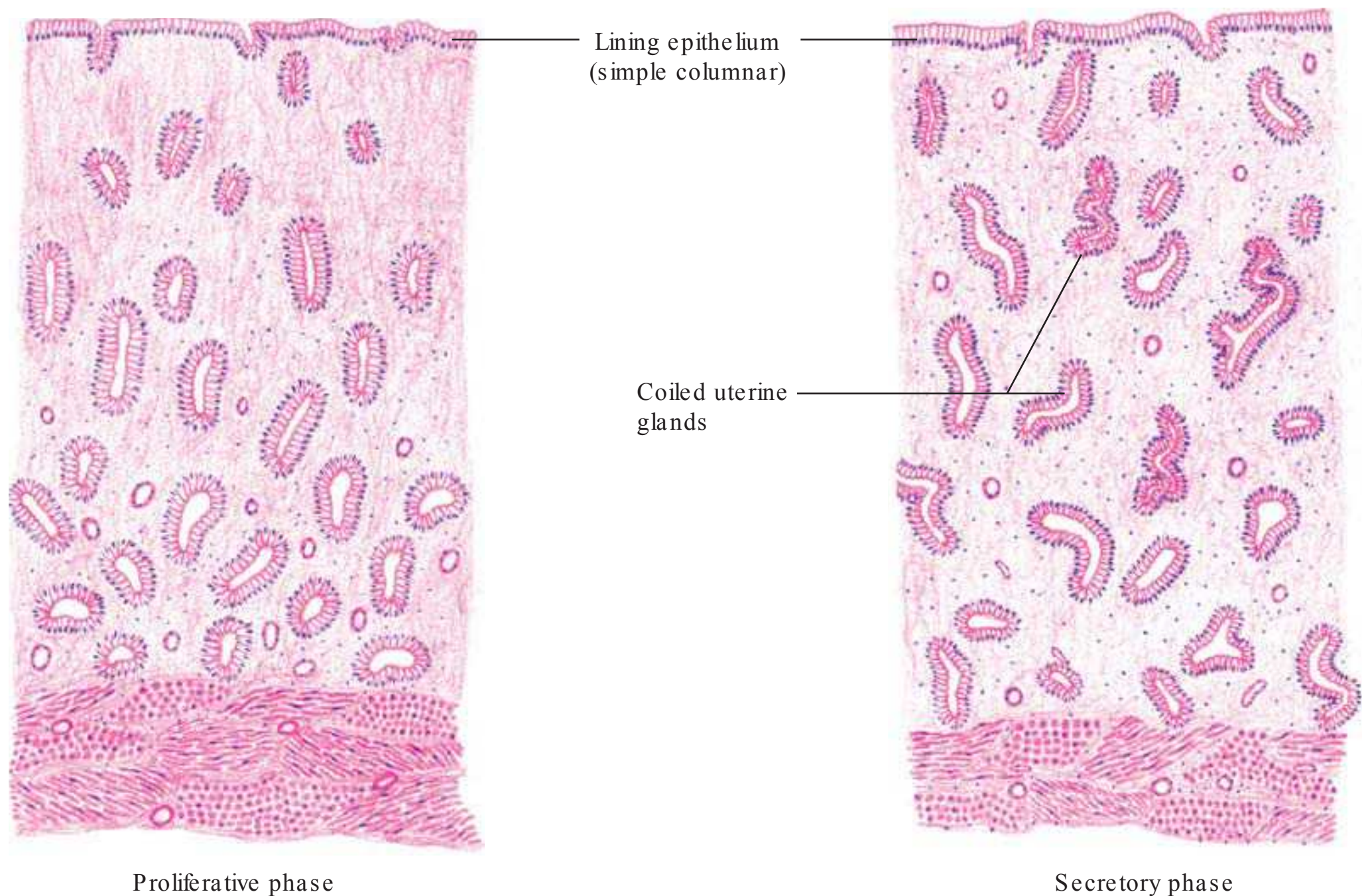


**CYCLICAL CHANGES IN ENDOMETRIUM (Figs 18.6 and 18.7)**

In the reproductive age group, the microscopic features of the stratum functionale undergo regular cyclical changes during the menstrual cycle. The changes are mainly seen in the thickness of the endometrium, the length and coiling of the arteries and the glands. The regular 28-day cycle has three phases: proliferative, secretory and menstrual.



**Figure 18.6** Sections of the uterus in low magnification: proliferative phase (on left) and secretory phase (on right). Note the increased thickness of stratum functionale and the coiling of the glands (saw-tooth appearance) in the secretory phase. (H&E pencil drawing)



**Figure 18.7** Sections of the uterus in medium magnification: proliferative phase (on left) and secretory phase (on right) (H&E pencil drawing).



### Proliferative Phase

- This phase begins after menstruation, from the 4th or 5th day to 14th day of the menstrual cycle.
- The events occurring in this phase are under the influence of the hormone oestrogen, which is secreted from the developing follicles in the ovary.
  - (a) The stratum functionale, which was shed during the menstrual phase, regenerates from stratum basale. The thickness of stratum functionale increases.
  - (b) The glands are straight, and they increase in length (Fig. 18.5).
  - (c) The spiral artery increases in length, but does not extend beyond basal two-thirds of the endometrium (Fig. 18.5).

### Secretory Phase

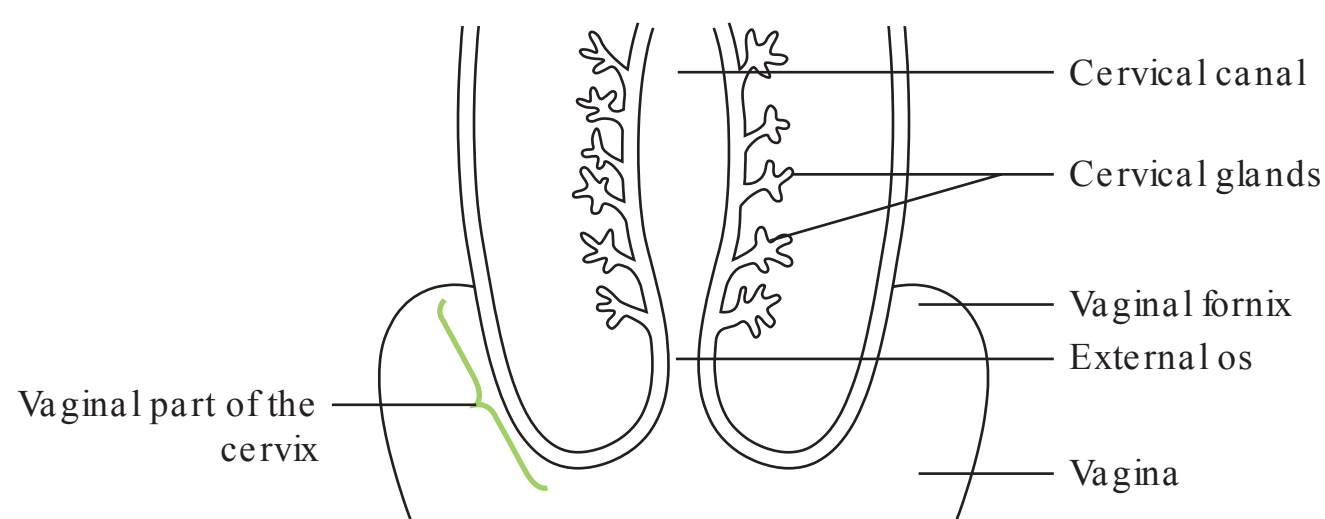
- This phase lasts from day 14 to day 28.
- Changes take place under the influence of progesterone secreted by the corpus luteum.
  - (a) Thickness of the endometrium increases further, and it almost doubles from what it was in the previous phase.
  - (b) Glands enlarge and become highly coiled (Fig. 18.5), characterised by 'saw-tooth appearance' in sections; their lumens are filled with secretions.
  - (c) The spiral arteries become more coiled, and they grow in length and extend into the superficial region of the stratum functionale (Fig. 18.5).

### Menstrual Phase

- This phase lasts from day 1 to day 4 or 5 of the menstrual cycle.
- The events occurring in this phase are due to decline in the progesterone level, which is due to degeneration of corpus luteum. Intermittent contractions occur in the spiral arteries; the stratum functionale is subjected to ischaemia and undergoes degeneration.
- The entire stratum functionale is shed. The menstrual fluid containing the necrotic tissue of stratum functionale and blood is discharged through the vagina.
- The straight arteries of stratum basale do not undergo constriction during this phase, and hence no ischaemic changes occur in stratum basale and it is not shed.

## CERVIX

- It is the part of the uterus below the isthmus (Fig. 18.1).
- A part of the cervix protrudes through the vagina; it is called the vaginal part of the cervix (Fig. 18.8). The vaginal part of the cervix is surrounded by a circular furrow, the vaginal fornix.
- The cervix encloses a narrow cervical canal, which communicates with the uterine cavity through the internal os and with the vagina through the external os.



**Figure 18.8** Cervix.

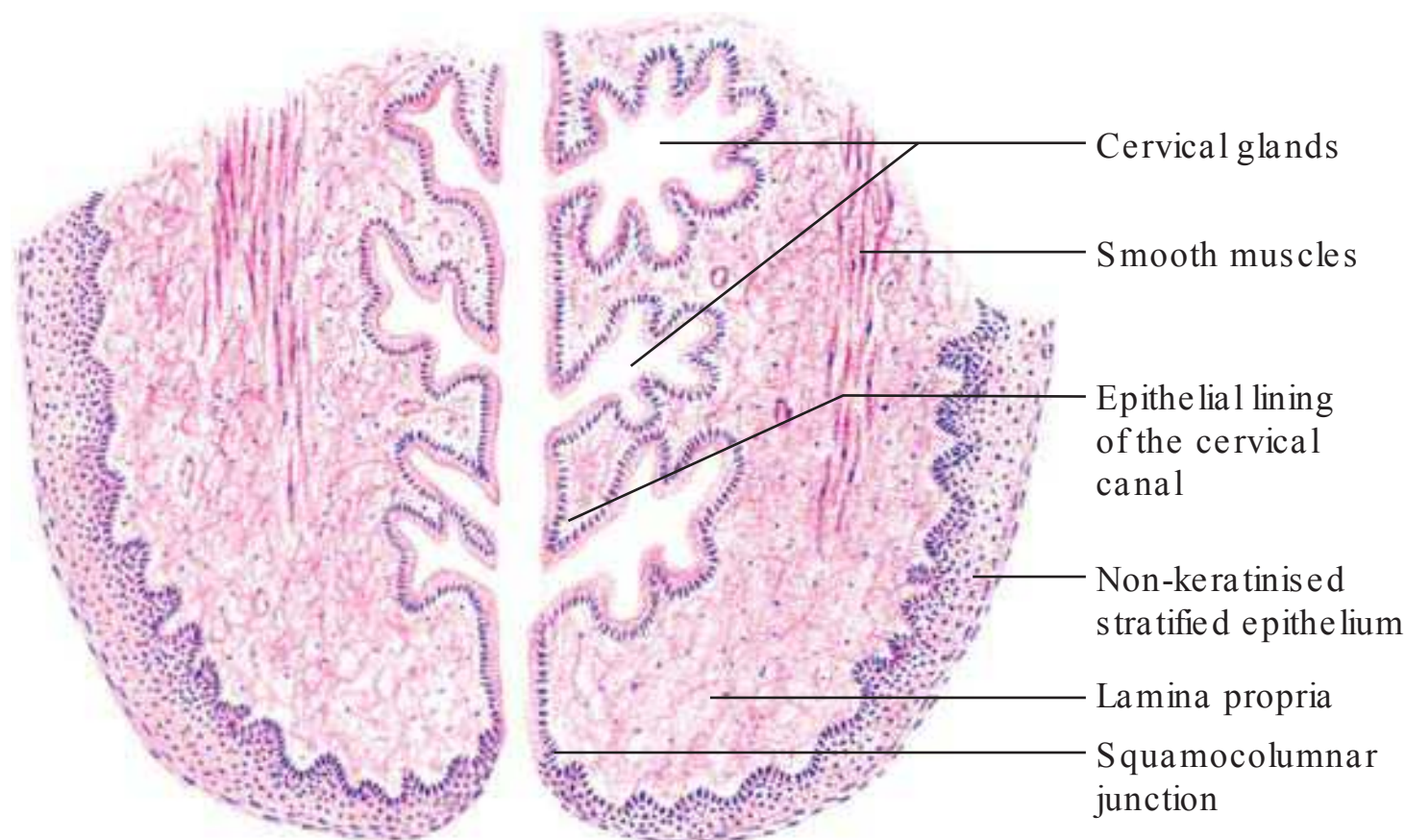


**MICROSCOPIC FEATURES** (Fig. 18.9)

- The mucosa lining the cervical canal consists of epithelium and lamina propria.
- Underneath the mucosa, there is the connective tissue which forms the bulk of the cervix; some smooth muscles are also present in it.

**Mucosa**

- The cervical canal is lined by simple columnar epithelium.
- Lamina propria consists of connective tissue with numerous mucus-secreting branched tubular glands (cervical glands). Secretory activity of these glands undergoes cyclical changes during the menstrual cycle. During the proliferative phase of the menstrual cycle their secretions are watery (to allow easier passage of the sperm), and during the secretory phase the secretions become highly viscous (to prevent the passage of the microorganism from the vagina into the cervix).
- At the external os, the epithelium abruptly changes to non-keratinised stratified squamous epithelium. It continues over the vaginal part of the cervix and further with the epithelium of the vagina. The site where the epithelium changes from simple columnar to non-keratinised stratified squamous is known as transformation zone (squamocolumnar junction) (Fig. 18.9).
- Transformation zone is the most common site of origin of carcinoma cervix.
- Cervical mucosa is not shed during menstruation.



**Figure 18.9** Longitudinal section of cervix in low magnification (H&E pencil drawing).

## VAGINA

The vagina is a fibromuscular tube extending from the vaginal part of the cervix to the external genitalia (Fig. 18.1).

## **MICROSCOPIC FEATURES**

Its wall consists of three layers (from inside to outside): the mucosa, muscularis and adventitia.

### **Mucosa**

- Mucosa consists of surface epithelium and lamina propria.
- Epithelium is non-keratinised stratified squamous epithelium.
- Lamina propria is composed of dense connective tissue.
- Vaginal mucosa is devoid of glands, and it is lubricated by mucus secreted by cervical glands.

### **Muscularis**

- Inner circular and outer longitudinal layers of smooth muscle are present.

### **Adventitia**

- The adventitia and contains many elastic fibres which contribute to the elasticity of the wall of the vagina.

## **MAMMARY GLAND**

- A pair of mammary glands (or breasts) is present in the pectoral region of both sexes, but in males it is rudimentary.
- It is a modified apocrine sweat gland located in the subcutaneous tissue.

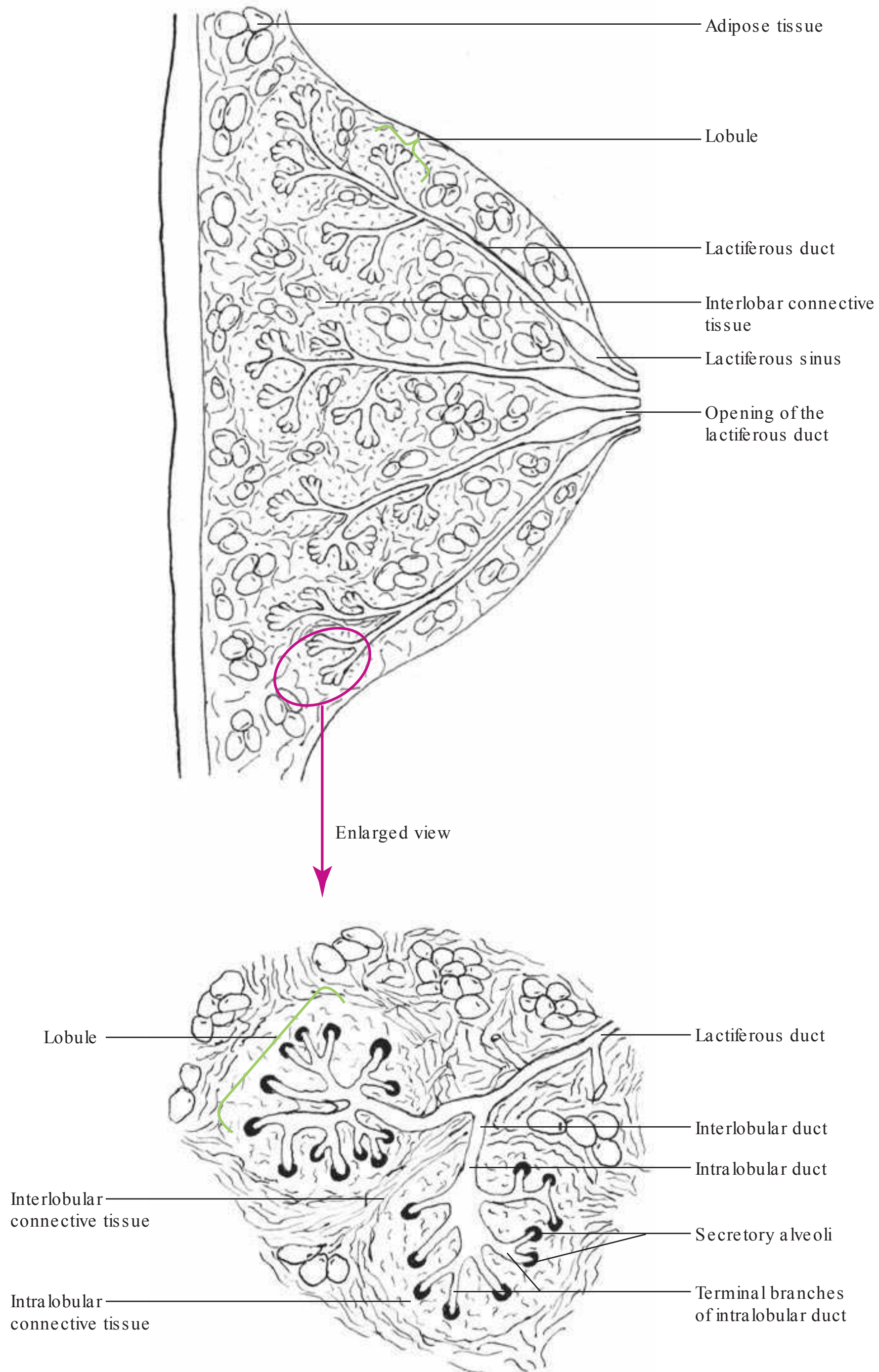
## **STRUCTURE OF THE RESTING MAMMARY GLAND**

- The resting mammary gland refers to the mammary gland of an adult female in non-pregnant state.
- Each mammary gland consists of 15–20 lobes, each lobe having a compound tubuloalveolar gland; ducts of these glands open on the nipple.

### **Lobes**

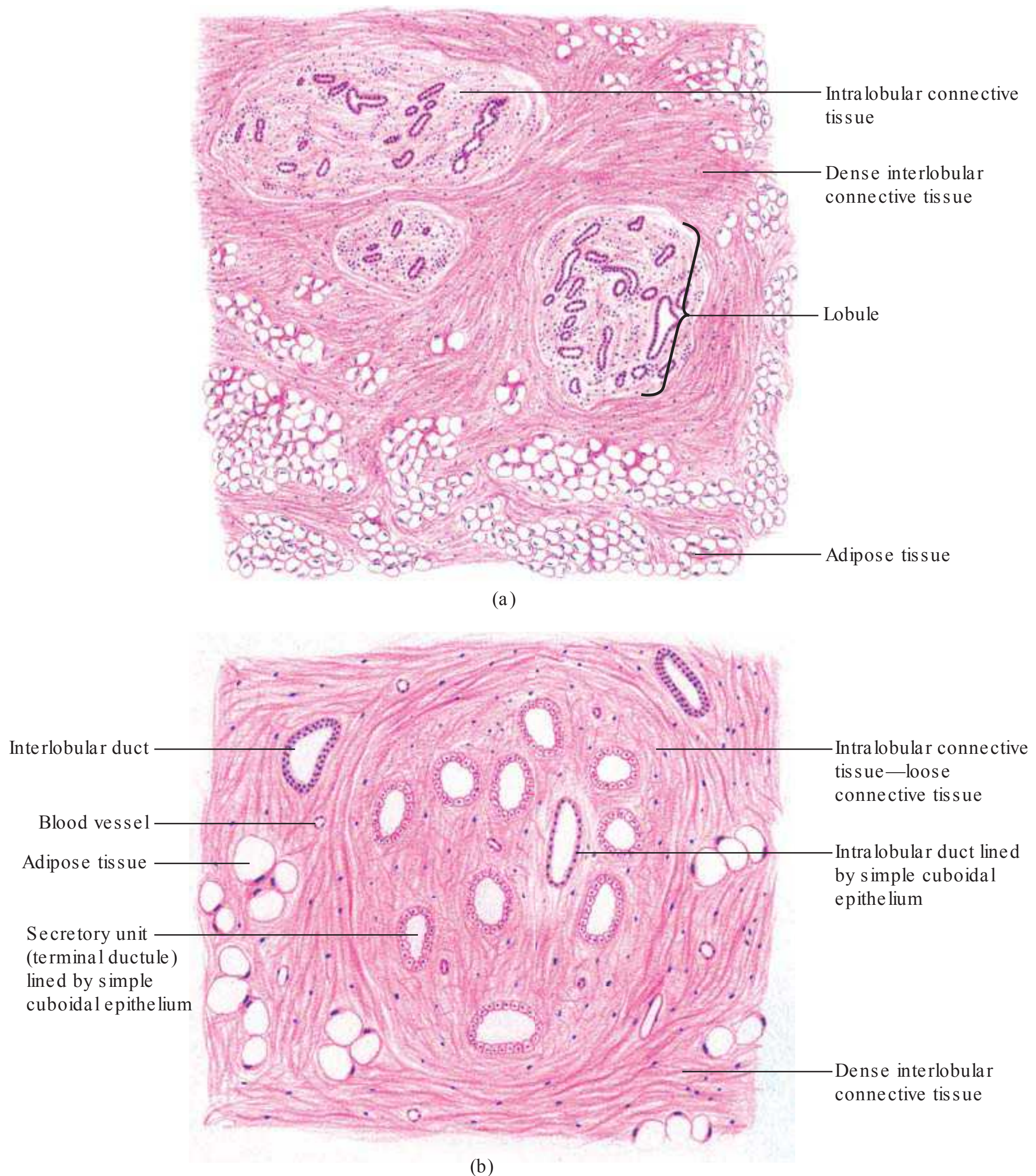
- As mentioned earlier, each mammary gland consists of 15–20 lobes; each lobe is separated from other lobes by dense interlobar connective tissue and fat.
- Each lobe is an individual gland (compound tubuloalveolar gland), and the duct of each lobe, known as lactiferous duct, has its own opening on the nipple.
- Each lobe is further divided into numerous lobules which are separated from each other by dense interlobular connective tissue (Figs 18.10 and 18.11; PMG 18.8).
- Within the lobule there is the intralobular loose connective tissue and several ducts. The intralobular connective tissue is devoid of fat.





**Figure 18.10** Schematic diagram showing general organisation of the female breast. In the upper diagram numerous lobes separated by interlobar connective tissue and lactiferous ducts can be seen. Inset shows an enlarged view of two lobules separated by interlobular connective tissue and intralobular ducts.



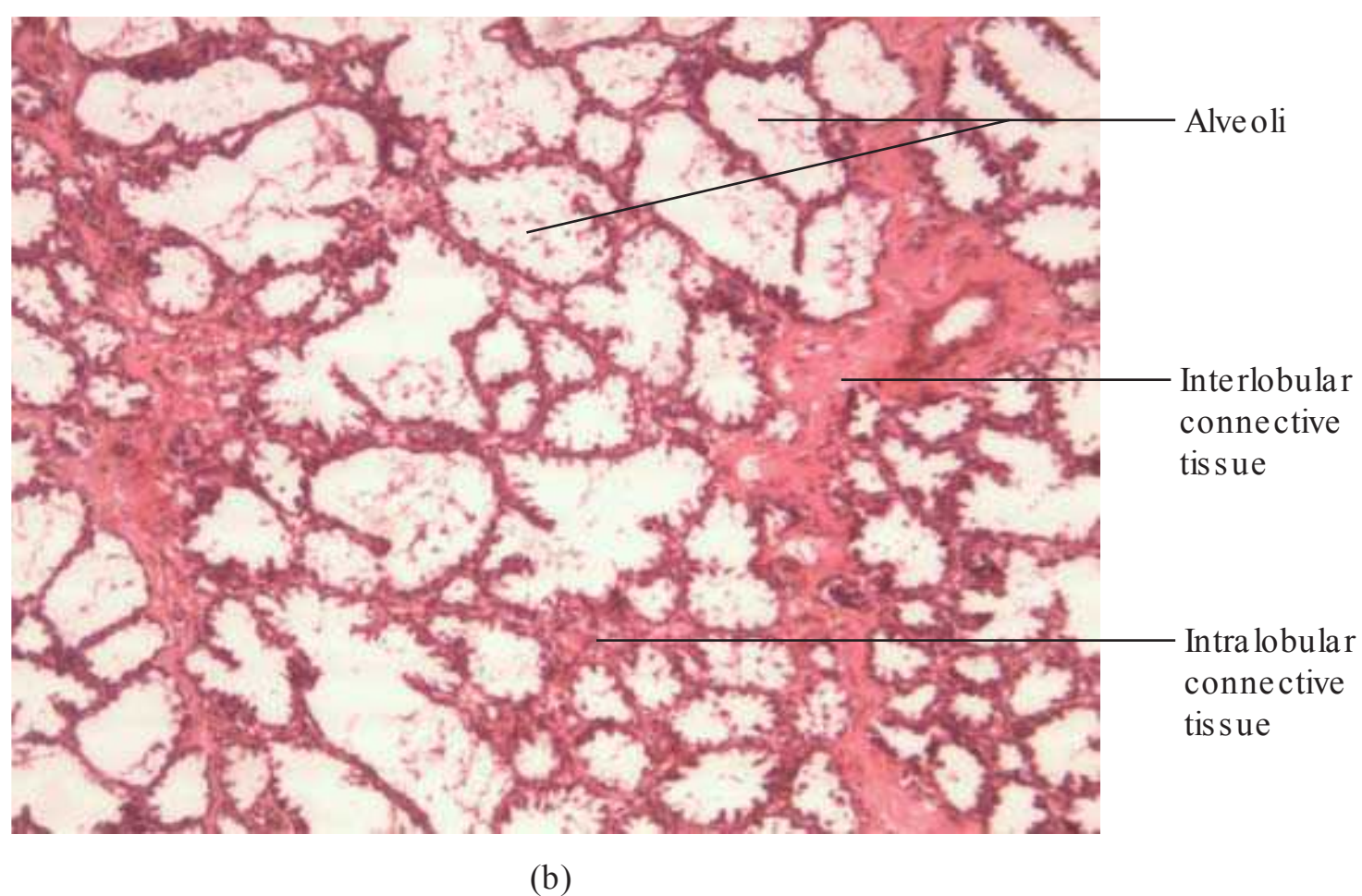
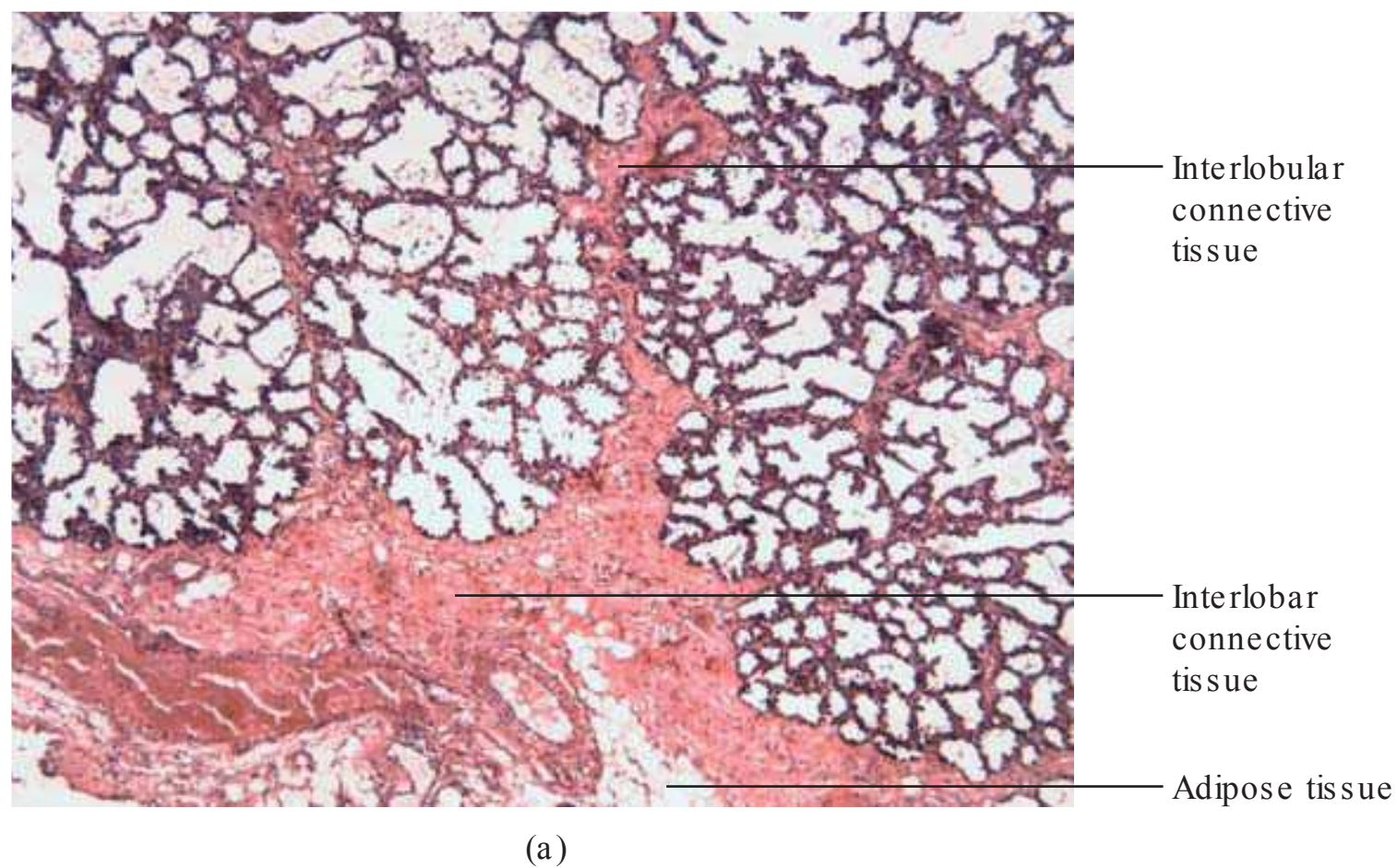


**Figure 18.11** Section of resting breast: (a) low magnification and (b) high magnification—one lobule surrounded by interlobular connective tissue can be seen (H&E pencil drawing).

### Duct System (Figs 18.10 and 18.12)

- Ducts within the lobule are called intralobular ducts.
- Intralobular ducts drain into interlobular ducts, which drain into the lactiferous duct.
- Beneath the nipple, the lactiferous duct dilates into lactiferous sinus, which functions as a reservoir of milk.
- Ducts are lined by epithelium. The type of epithelium varies in different parts of the duct system. The change in the epithelium occurs gradually. Smaller ducts are lined by simple cuboidal or columnar epithelium, while larger ducts are lined by two-layer thick cuboidal or columnar epithelium. A lactiferous duct near its opening is lined by stratified squamous keratinised epithelium (Fig. 18.12).
- Between the epithelium and the basement membrane of the ducts, myoepithelial cells are present.





**PMG 18.8** Breast: (a) X5 and (b) X10 (H&E stain).

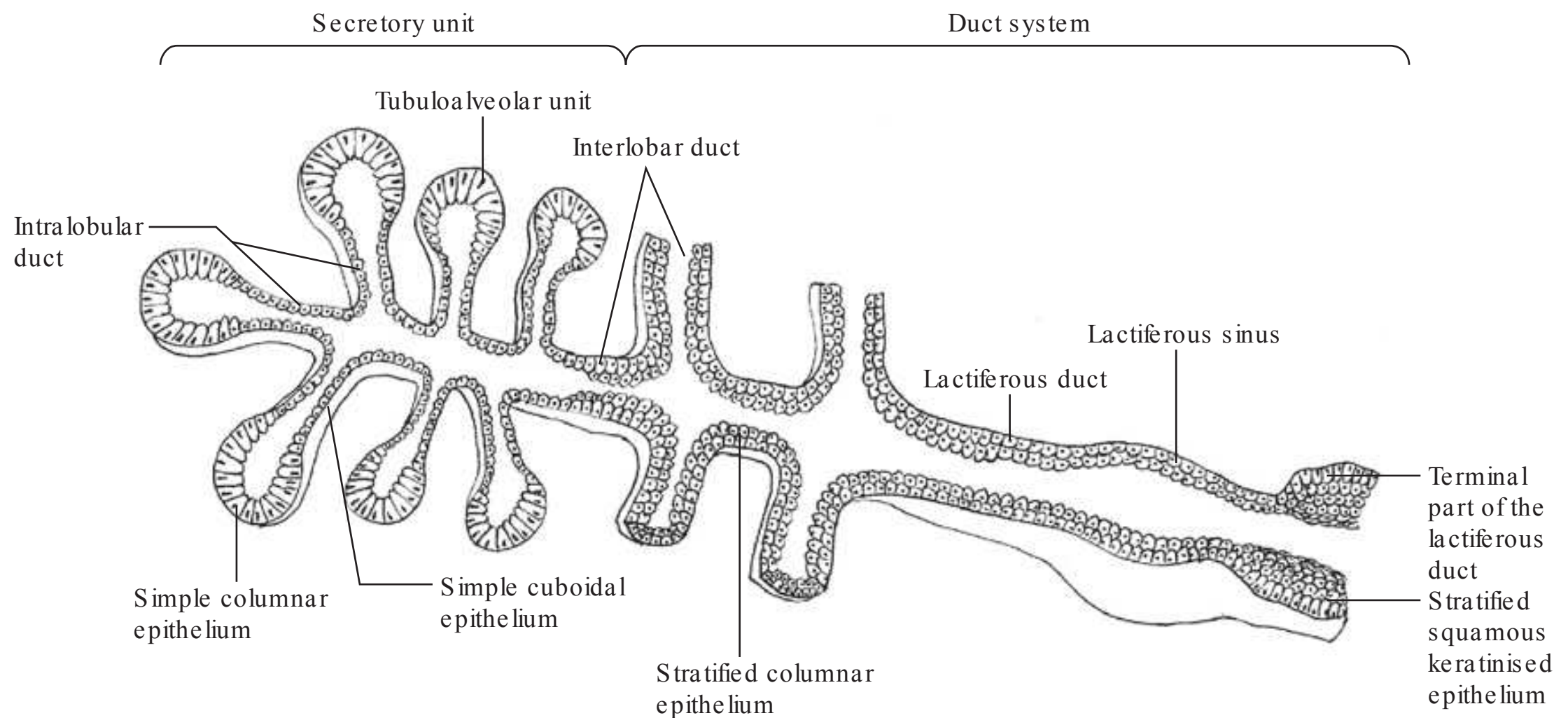
### Secretory Part

- Secretory units are inactive terminal branches of the intralobular duct and are lined by simple cuboidal or columnar epithelium (Figs 18.11b and 18.12).
- Myoepithelial cells are present between the glandular cells and the basement membrane.

### Nipple and Areola

- The nipple is covered by keratinised stratified squamous epithelium.
- It consists of dense connective tissue and smooth muscles arranged circularly and longitudinally.
- The pigmented skin around the nipple is called areola. The skin lacks hair follicles and numerous sebaceous glands are present.

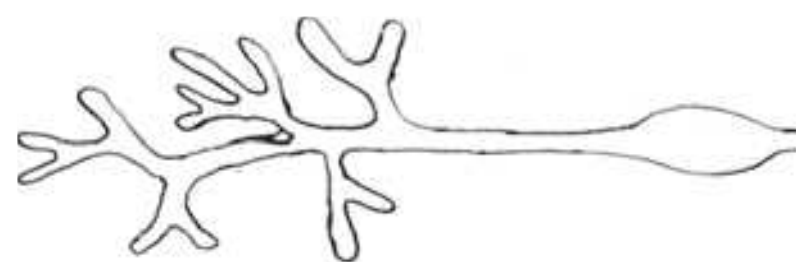




**Figure 18.12** The lining epithelium of the secretory unit and duct system of a lobe—15–20 such lobes are present in a mammary gland and each lobe has several lobules (only one lobule is shown here—note the cut ends of the interlobar ducts of other lobules).

### BREAST DURING PREGNANCY

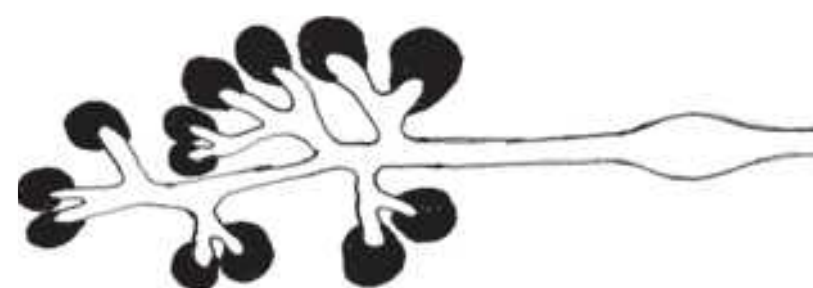
- The hormonal changes during pregnancy (elevated levels of oestrogen and progesterone) induce formation of new terminal branches of ducts. Secretory alveoli develop at the ends of the terminal branches of the ducts. These changes are seen in the first half of pregnancy.
- Apart from the changes in the duct system, there is reduction in the amount of intra- and interlobular connective tissue (Figs 18.13 and 18.14).



Resting stage—inactive ducts



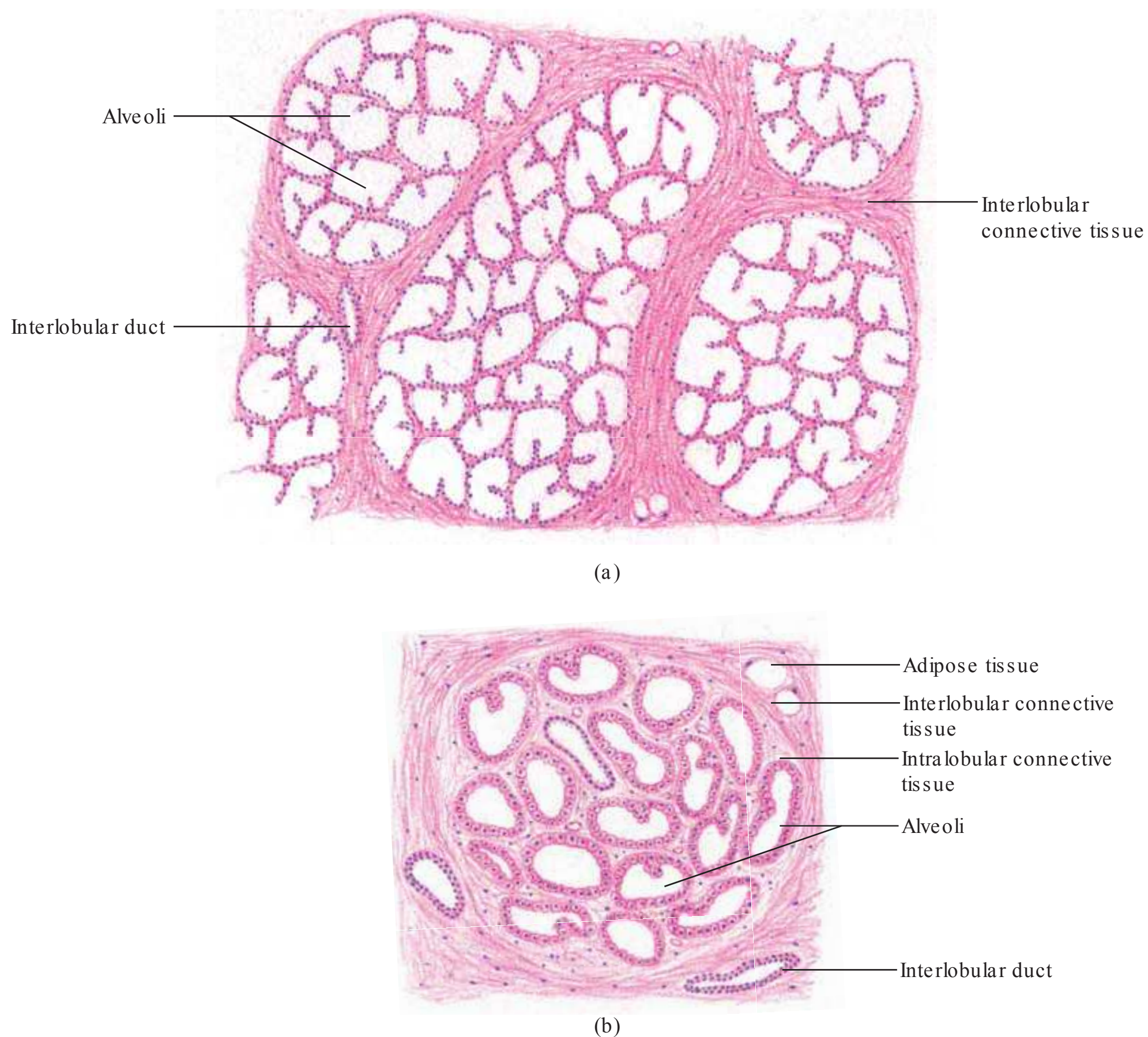
During pregnancy—proliferating new ductules and alveoli



During lactation—distended alveoli filled with milk

**Figure 18.13** Changes in the mammary gland during pregnancy and lactation. The mammary gland in the resting stage has also been shown.





**Figure 18.14** Section of breast during pregnancy: (a) low magnification—lobules packed with secretory alveoli can be seen—and (b) high magnification (H&E pencil drawing).

## LACTATING BREAST

- Secretory cells become low cuboidal.
- Alveoli are distended and filled with milk (Fig. 18.13).

## CLINICAL CORRELATES

### Ovarian Tumours

- Ovarian tumours arise from one of the three components of the ovary, that is the surface epithelium, the germ cells and the stroma. Tumours arising from the surface epithelium are most common.

### Endometriosis

- Endometriosis is characterised by the presence of endometrial tissue outside the uterus. Common symptoms are dysmenorrhoea and infertility.

### Leiomyomas

- These are benign tumours of myometrium, also called fibroids. These are often multiple solid nodules and show whorled appearance of smooth muscles on the histological section. Rarely, it turns malignant (leiomyosarcoma).

Pap Smear

- It is the screening test for cervical cancer. This test is an effective, widely used method for early detection of premalignant and malignant changes of the cervix. Surface scraping is done by a wooden spatula, around the external os. The cells in the scraping are studied under the microscope.

Breast Cancer

- It arises from epithelial cells lining the ducts and lobules of the breast. It is one of the most common cancers in females.

KEYPOINTS

Ovary (Fig. 18.2; PMG 18.1)

Each ovary consists of the following two parts:

- Cortex—connective tissue with ovarian follicles
- Medulla—connective tissue with numerous blood vessels
- Overlying the cortex is germinal epithelium and tunica albuginea

Different Types of Follicles (Figs 18.2 and 18.3; PMG 18.2)

Follicles	Features
Primordial	<ul style="list-style-type: none"><li>• Ova surrounded by a single layer of flat follicular cells</li></ul>
Primary	<ul style="list-style-type: none"><li>• Flat follicular cells become cuboidal—unilaminar primary follicle</li><li>• Zona pellucida is formed</li><li>• Follicular cells become multilayered—multilaminar primary follicle</li><li>• Surrounding the follicle is theca interna and theca externa</li></ul>
Antral/secondary follicle	<ul style="list-style-type: none"><li>• Small cavities appear in between follicular cells</li></ul>
Graafian follicle	<ul style="list-style-type: none"><li>• One large antrum</li><li>• Ovum on one side of follicle</li><li>• Corona radiata—cells surrounding the ovum</li><li>• Cumulus oophorus—cells concentrate at one point on which ovum rests</li></ul>

Fallopian Tube

- It consists of three layers: mucosa, muscular layer and serosa (Fig. 18.4; PMG 18.5).
- The epithelium has two types of cells: ciliated cells and non-ciliated secretory cells.
- The muscular layer consists of inner circular and outer longitudinal smooth muscle layers.

Uterus

- It has three layers: endometrium, myometrium and serosa or adventitia (perimetrium).
- The endometrium is divided into two layers: stratum functionale and stratum basale (Figs 18.6 and 18.7; PMG 18.6). The stratum functionale is shed during menstruation.

Cyclical Changes in Endometrium

Proliferative phase (Figs 18.5–18.7)	Secretory phase (Figs 18.5–18.7)
From day 5 to day 14	From day 14 to day 28
Under the influence of oestrogen	Under the influence of progesterone
Stratum functionale regenerates from stratum basale	Thickening of the endometrium
Glands increase in length	Glands become coiled—‘saw-tooth appearance’; coiled arteries grow in length



**Cervix (Fig. 18.9)**

- The mucosa lining the cervical canal consists of epithelium (simple columnar) and lamina propria.
- At the external os, the epithelium abruptly changes to non-keratinised stratified squamous epithelium. The site of change of epithelium is known as transformation zone.

**Mammary Gland (Figs 18.10–18.12; PMG 18.8)**

It is a modified apocrine sweat gland. It consists of parenchyma, stroma and duct system.

**Parenchyma**

- It has 15–20 lobes, each lobe having a compound tubuloalveolar gland.
- Secretory units are terminal ductules of the intralobular ducts and are lined by simple cuboidal or columnar epithelium.

**Stroma**

- It consists of interlobar, interlobular and intralobular connective tissue.

**Duct System**

- Terminal ductules → intralobular ducts → interlobular ducts → lactiferous ducts → opens on the nipple.
- Smaller ducts are lined by simple cuboidal or columnar epithelium, while larger ducts are lined by two-layer thick cuboidal or columnar epithelium. A lactiferous duct near the opening is lined by stratified squamous keratinised epithelium.

**SELF-ASSESSMENT**

1. Describe briefly the coverings of the ovary.
2. Compare the structures of the different types of follicles in the ovary.
3. What is corpus luteum?
4. Name the different layers of the wall of the fallopian tube.
5. What are the different layers of the wall of the uterus?
6. What are stratum functionale and stratum basale? Discuss the cyclical changes seen in them during menstrual cycle.
7. What do you understand by the transformation zone of the cervix?
8. Describe the structure of a lobe of the mammary gland.
9. What are the different types of ducts in the mammary gland? Mention their lining epithelium.
10. What are the histological changes seen in the mammary gland during pregnancy and lactation?

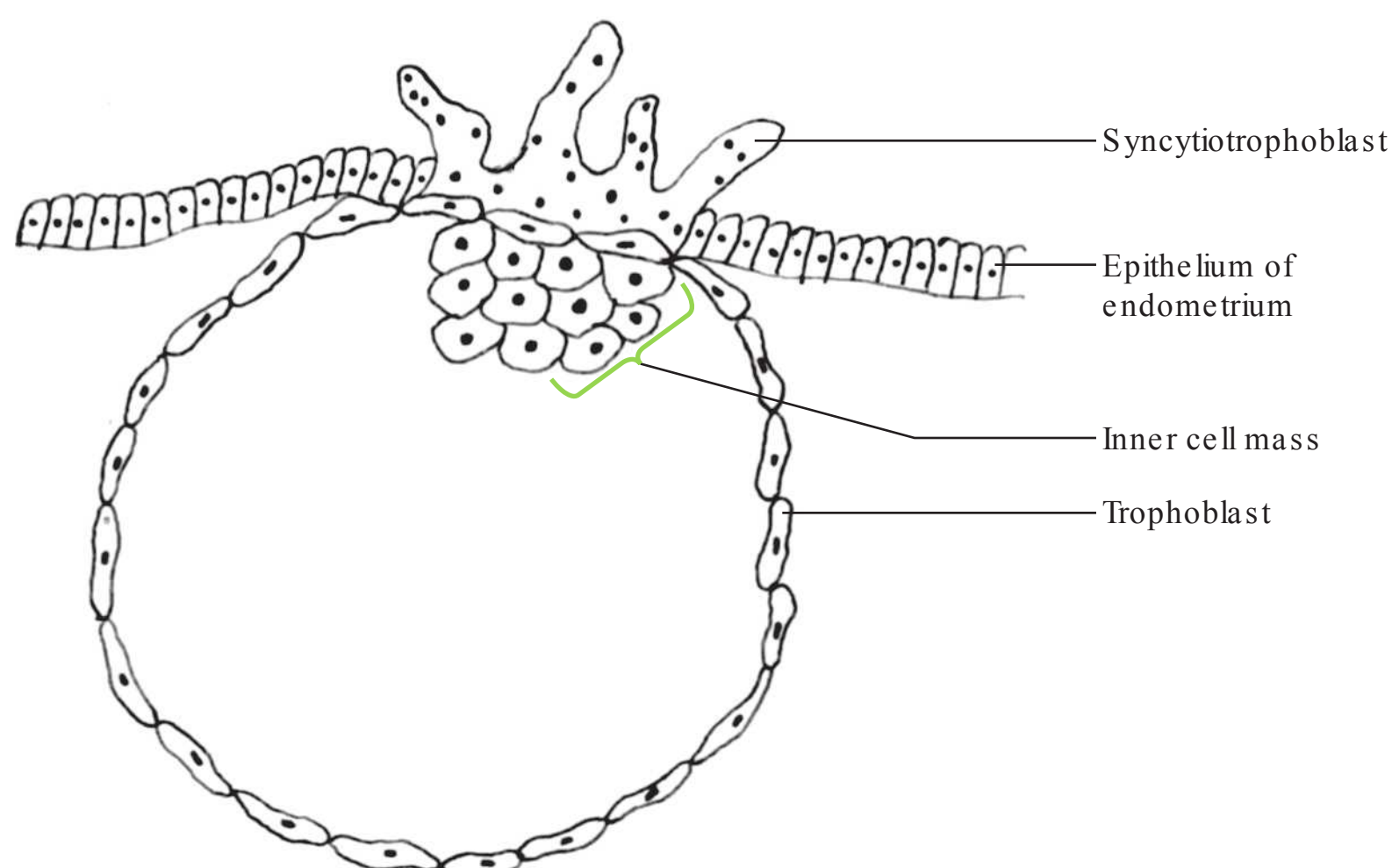
# Placenta and Umbilical Cord

## PLACENTA

- The placenta is a temporary organ; it consists of two parts: maternal and foetal (described later in the chapter).
- Functions
  - (a) Oxygen and nutrients are transported from the maternal to the foetal blood and foetal metabolic waste products and carbon dioxide from the foetal to the maternal blood. These substances pass freely across the placental barrier.
  - (b) Maternal IgG antibodies are transferred to the foetus. These antibodies confer passive immunity to the foetus.
  - (c) Endocrine functions: Syncytiotrophoblast secretes following hormones: human chorionic gonadotropin (hCG), oestrogen, progesterone and placental lactogen.

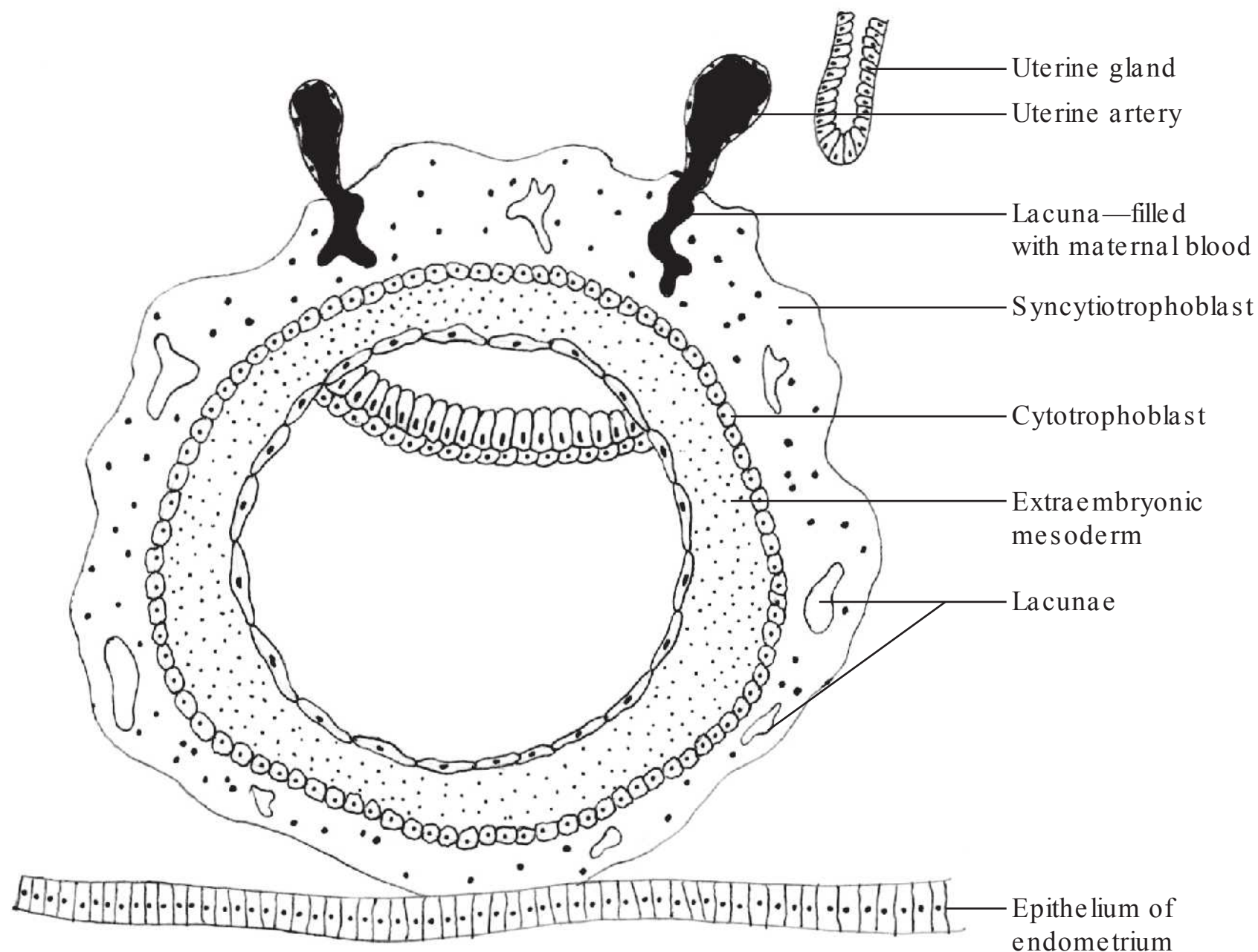
## DEVELOPMENT OF PLACENTA

- The development of the placenta begins with implantation of blastocysts. The trophoblast differentiates into inner cytotrophoblast and outer syncytiotrophoblast (Fig. 19.1). The cytotrophoblast consists of a single layer of cells. The syncytiotrophoblast consists of multiple cells without cell membrane.
- The syncytiotrophoblast erodes the endometrium and the blood vessels present in it (Figs 19.1 and 19.2).



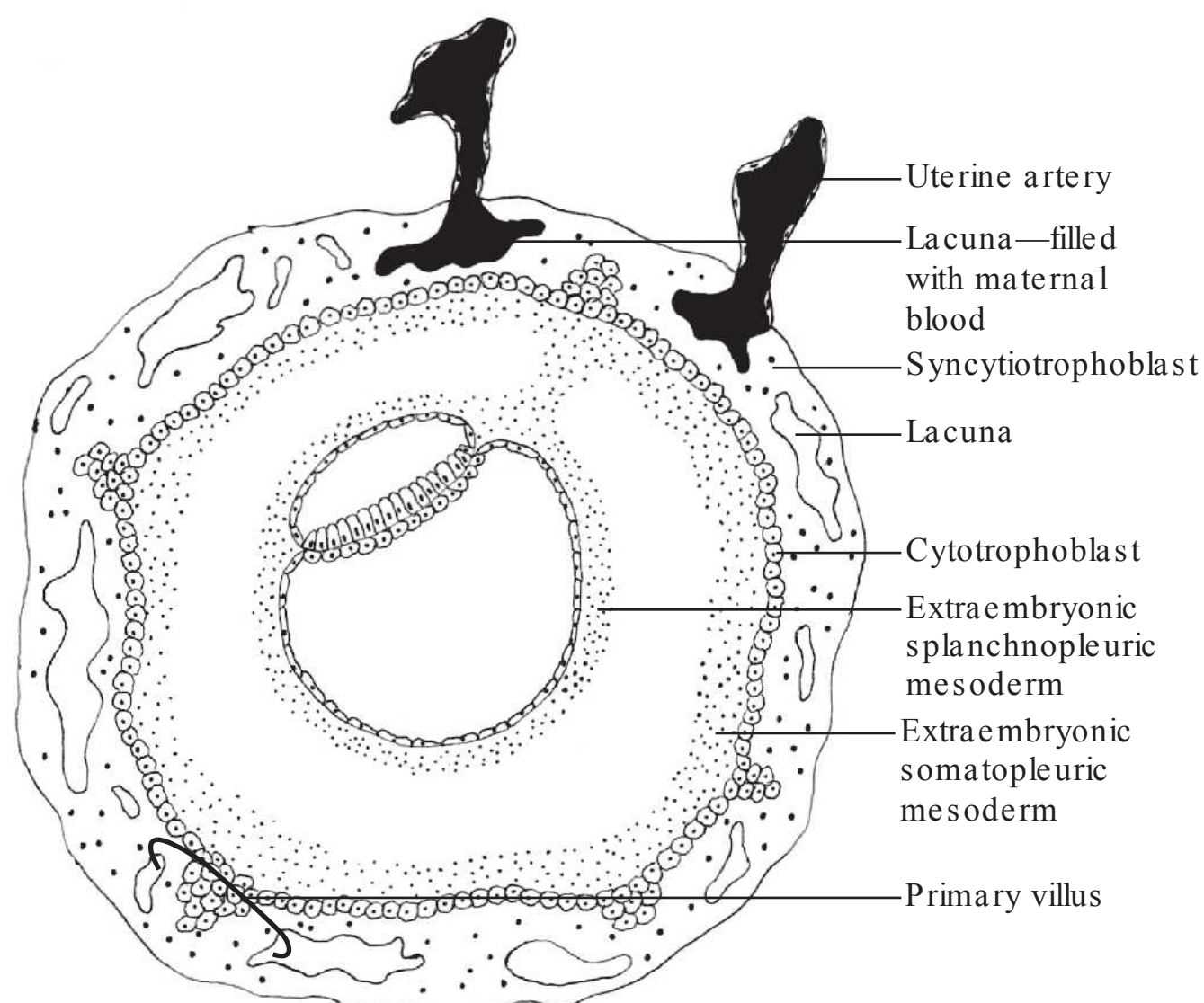
**Figure 19.1** Embryo at 7 days of development. Syncytiotrophoblast has begun to invade the endometrium.





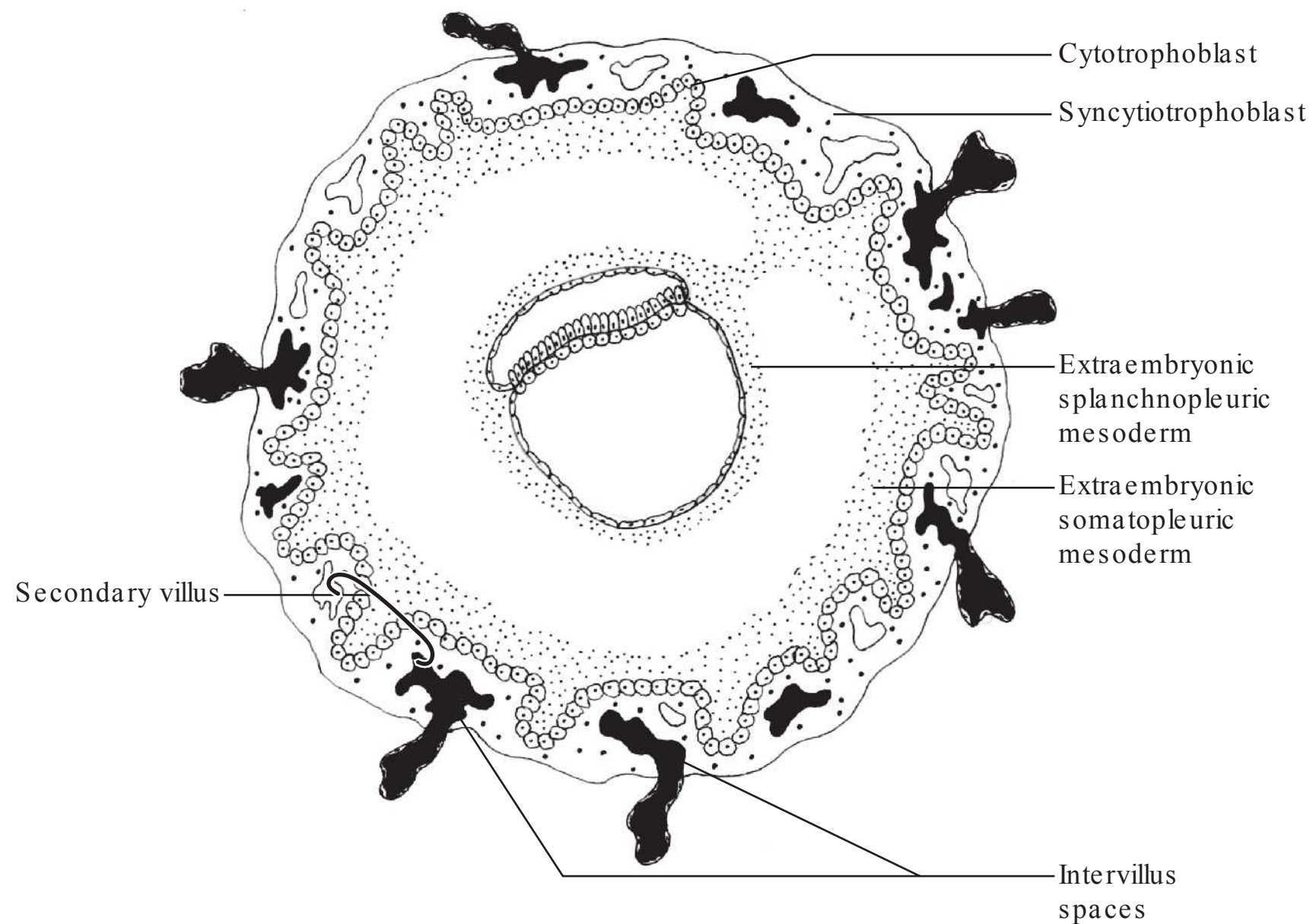
**Figure 19.2** Embryo at 9 days of development. Numerous lacunae are formed in syncytiotrophoblast.

- As the syncytiotrophoblast grows, intercommunicating spaces appear in it; these spaces are called lacunae (Fig. 19.2). Adjacent lacunae communicate with each other around the strands of syncytiotrophoblast. Meanwhile, a new layer of cells develops on the inner aspect of the cytotrophoblast known as extraembryonic mesoderm (Fig. 19.2). Soon, it splits into two layers: the extraembryonic somatopleuric mesoderm and extraembryonic splanchnopleuric mesoderm (Figs 19.3 and 19.4). The syncytiotrophoblast, cytotrophoblast and extraembryonic somatopleuric mesoderm together form the chorion.



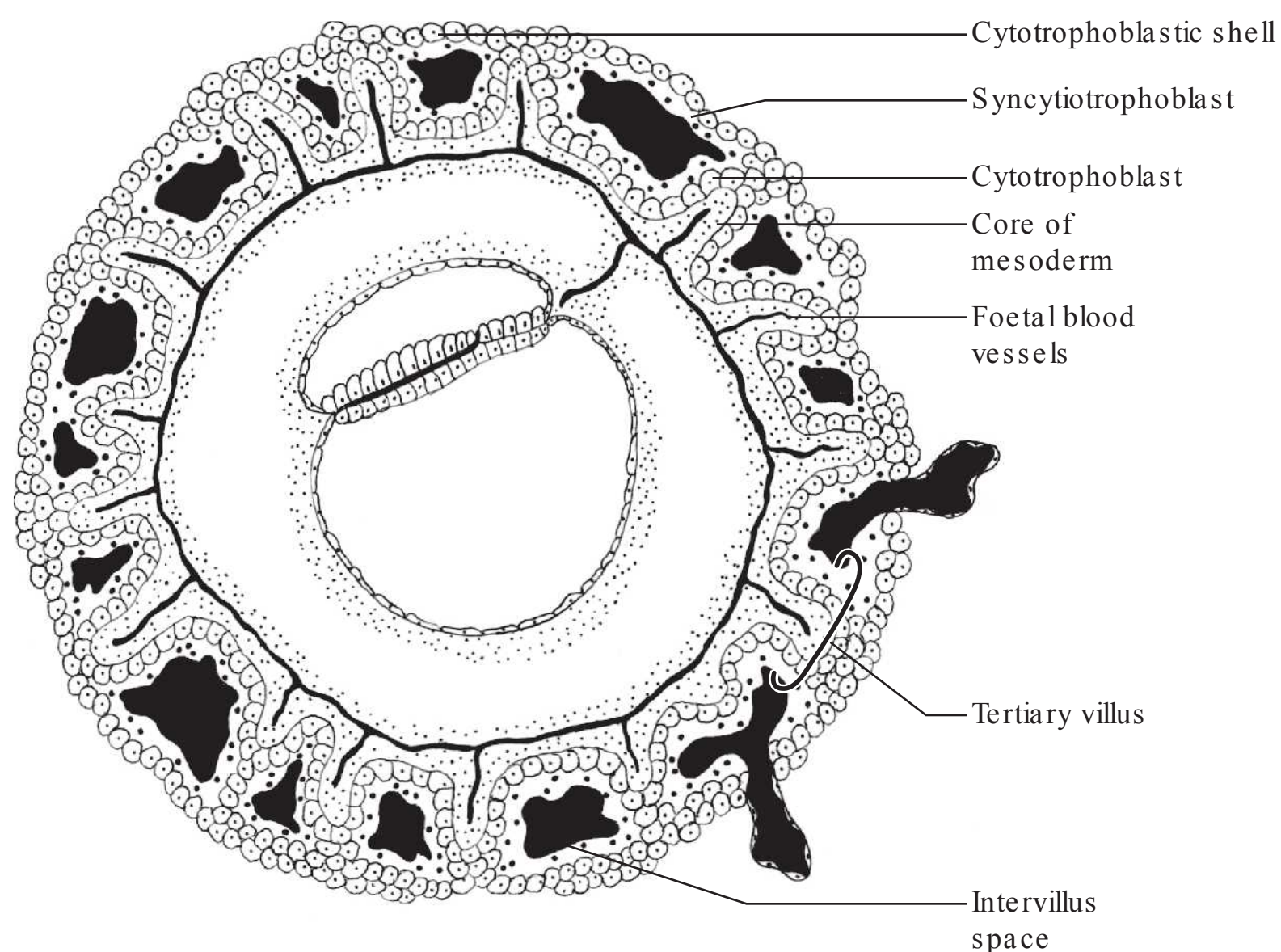
**Figure 19.3** Embryo at 13 days of development—formation of primary villi.





**Figure 19.4** Embryo at 16 days of development—formation of secondary villi.

- The cytotrophoblast invades the strands of syncytiotrophoblast and converts it into primary villi (Fig. 19.3). The maternal blood from the eroded maternal blood vessels fills the lacunae, which are referred to as intervillous spaces (Fig. 19.4). Initially villi develop all around the chorion, and later, all the villi undergo degeneration except the villi adjacent to the decidua basalis where they continue to grow. This portion of the chorion forms the foetal component (chorionic frondosum) of the placenta (see Fig. 19.8).
- An external layer of cytotrophoblast, the outer cytotrophoblast shell, is formed in the maternal part of the placenta (Fig. 19.5).



**Figure 19.5** Embryo at 21 days of development—formation of tertiary villi.



## VIII

- The foetal part of the placenta is connected with the maternal part by chorionic villi.
- There are three stages of chorionic villi: primary, secondary and tertiary (Fig. 19.6).

### Primary Villus

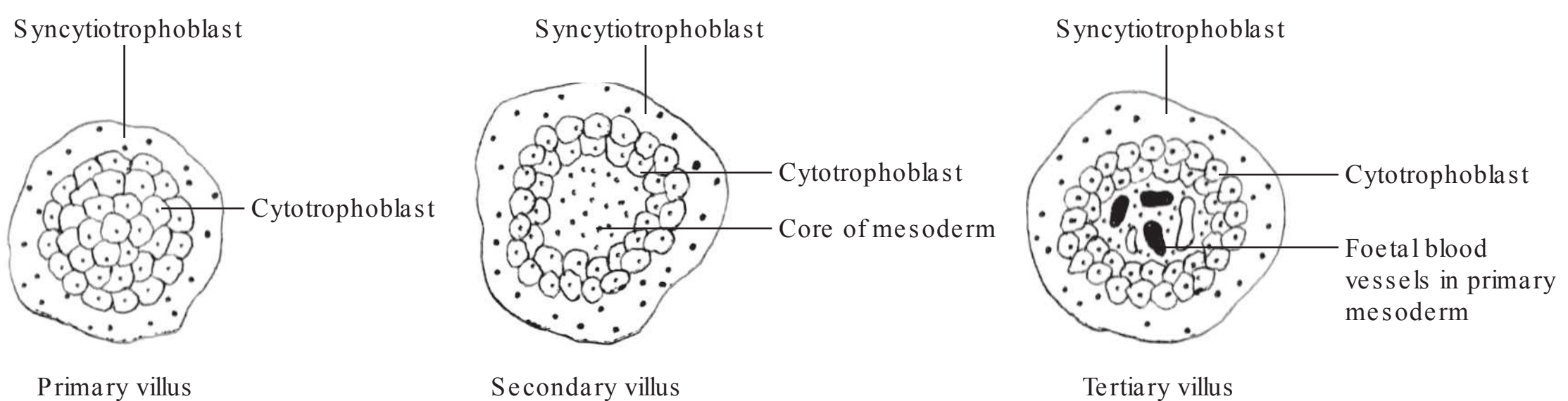
- It has a central core of cytotrophoblast, surrounded by syncytiotrophoblast (Figs 19.3 and 19.6)

### Secondary Villus

- The primary mesoderm invades the primary villi and forms the central core. The secondary villi have a central core of mesoderm surrounded successively by cytotrophoblast and syncytiotrophoblast (Figs 19.4 and 19.6).

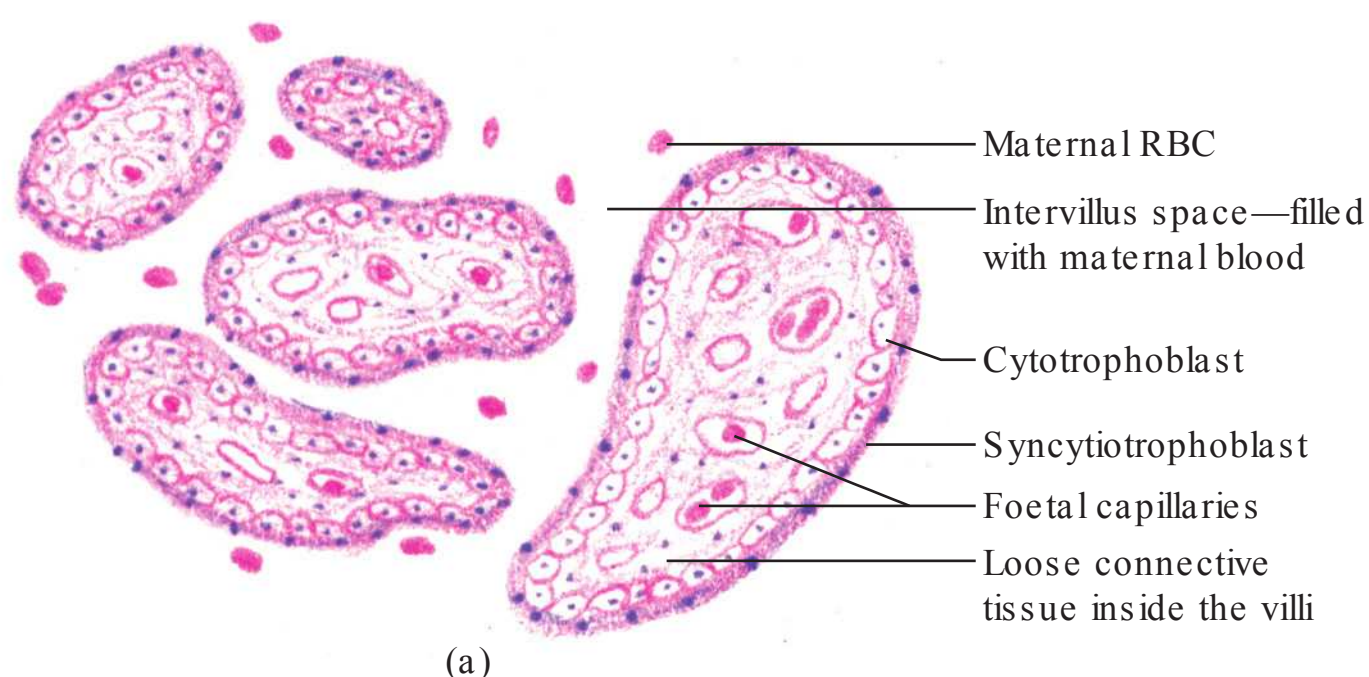
### Tertiary Villus

- With formation of foetal blood vessels in the central core of mesoderm, secondary villi are converted into tertiary villi (Figs 19.5 and 19.6).



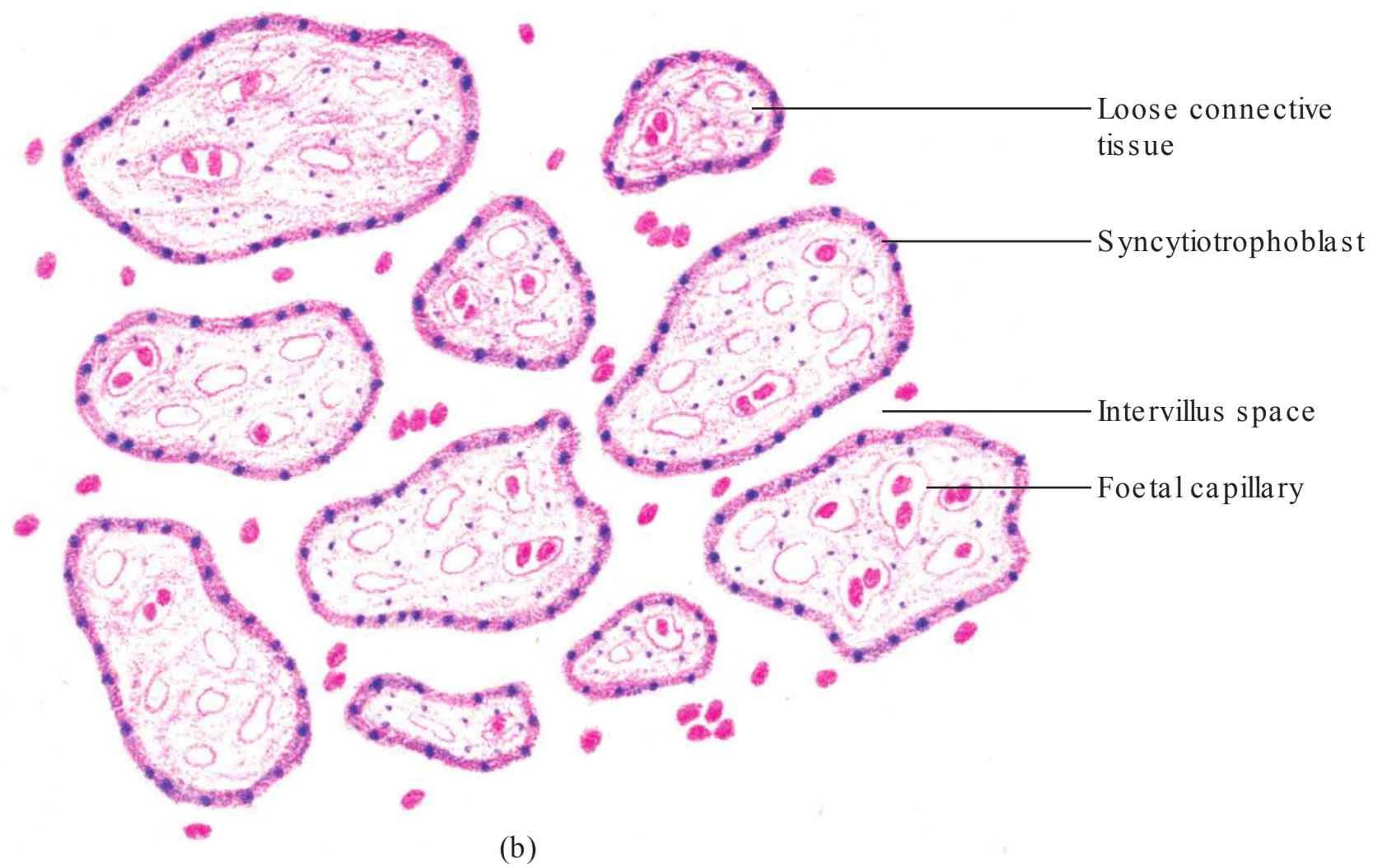
**Figure 19.6** Chorionic villi.

- The core of tertiary villi has loose connective tissue with foetal capillaries (Fig. 19.7a), fibroblasts and a few phagocytic cells called cells of Hofbauer. Hofbauer cells are large cells with large nuclei.
- The connective tissue is surrounded by syncytiotrophoblasts on the outer aspect which are darkly stained, and cytotrophoblasts on the inner aspect which are lightly stained in H&E preparation (Fig. 19.7a).
- In the later part of pregnancy (after third month), cytotrophoblasts progressively disappear (Fig. 19.7b; PMG 19.1).

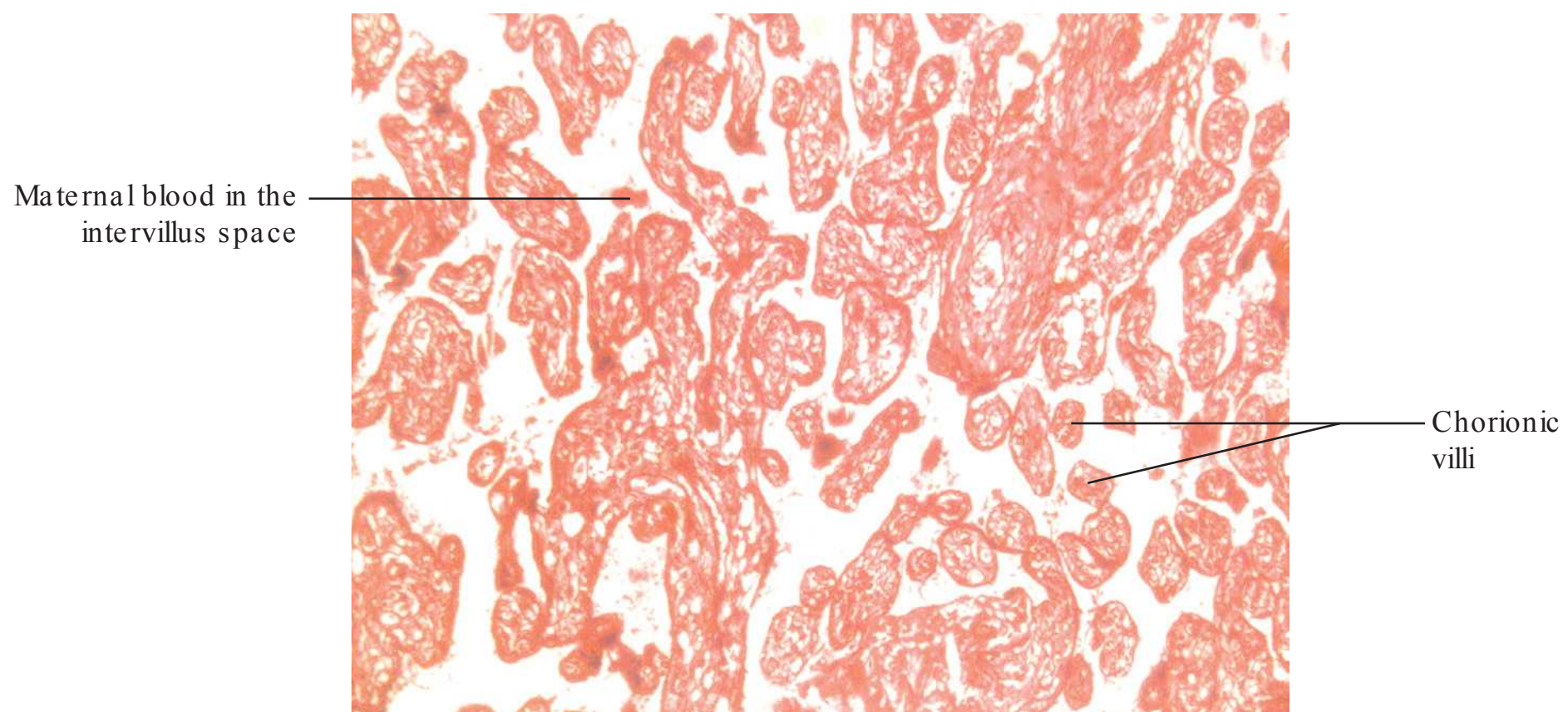


**Figure 19.7** (a) Section of placenta in low magnification at early stage of pregnancy (H&E pencil drawing). (continued)





**Figure 19.7** (continued) (b) Section of placenta at term—note the disappearance of cytotrophoblast (H&E pencil drawing).



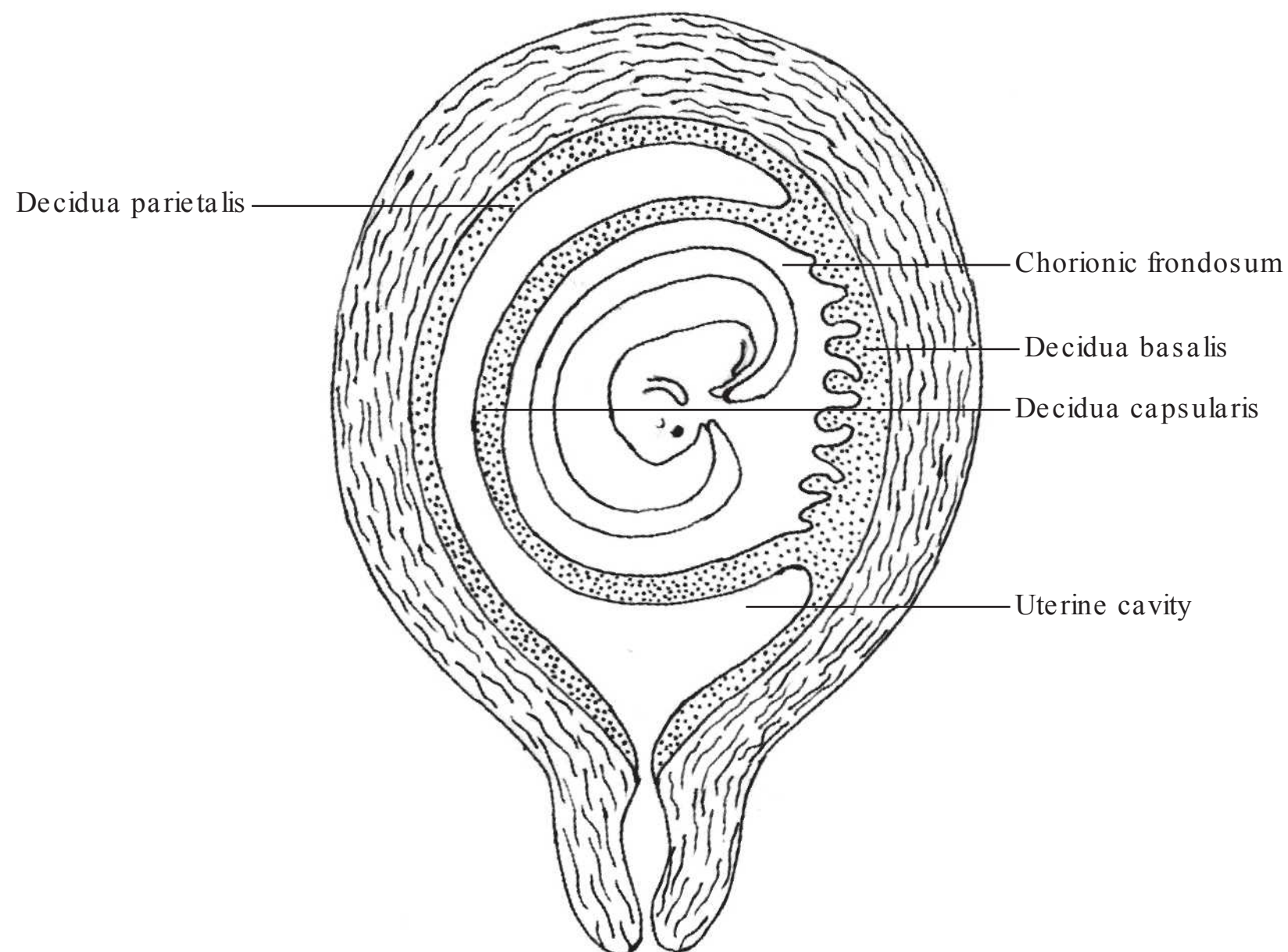
**PMG 19.1** Placenta at term. Numerous chorionic villi surrounded by intervillous space which contains maternal blood can be seen (H&E pencil drawing).

### DECIDUA (Fig. 19.8)

- The part of the endometrium which is shed during parturition is known as decidua.
- The cells of the endometrium increase in size and they become round in shape; these changes are known as decidualisation. Decidualisation begins at the site of implantation and spreads to the remaining endometrium.



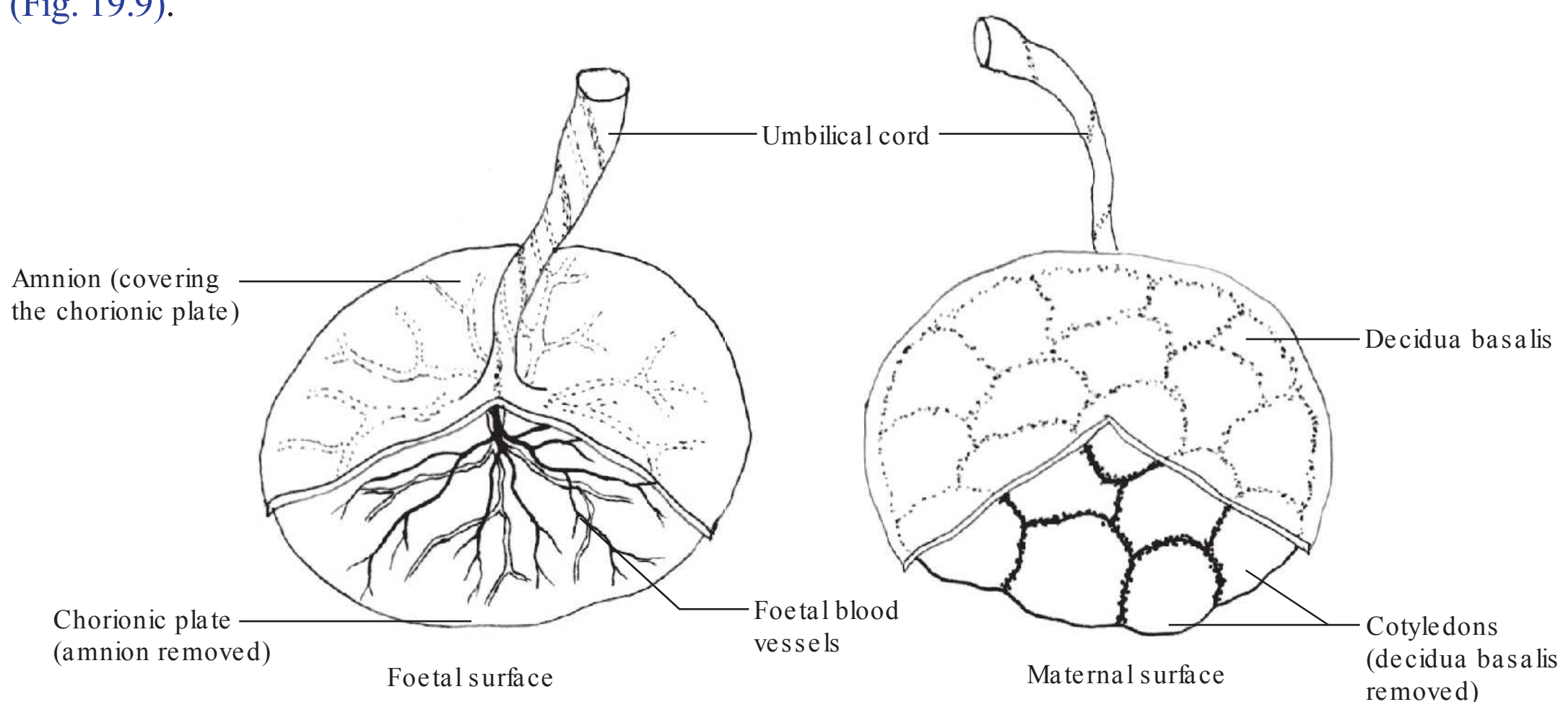
- The entire decidua consists of three different parts: decidua basalis, decidua capsularis and decidua parietalis.
- The decidua underlying the site of implantation is decidua basalis, which forms the maternal part of the placenta. The wedge-shaped extensions of decidua basalis towards the foetal part of the placenta form the placental septa (Figs 19.9 and 19.10).
- The thin layer of decidua overlying the implanted embryo is called decidua capsularis.
- The decidua lining the rest of the uterine cavity is known as decidua parietalis.



**Figure 19.8** Parts of decidua.

### STRUCTURE OF PLACENTA

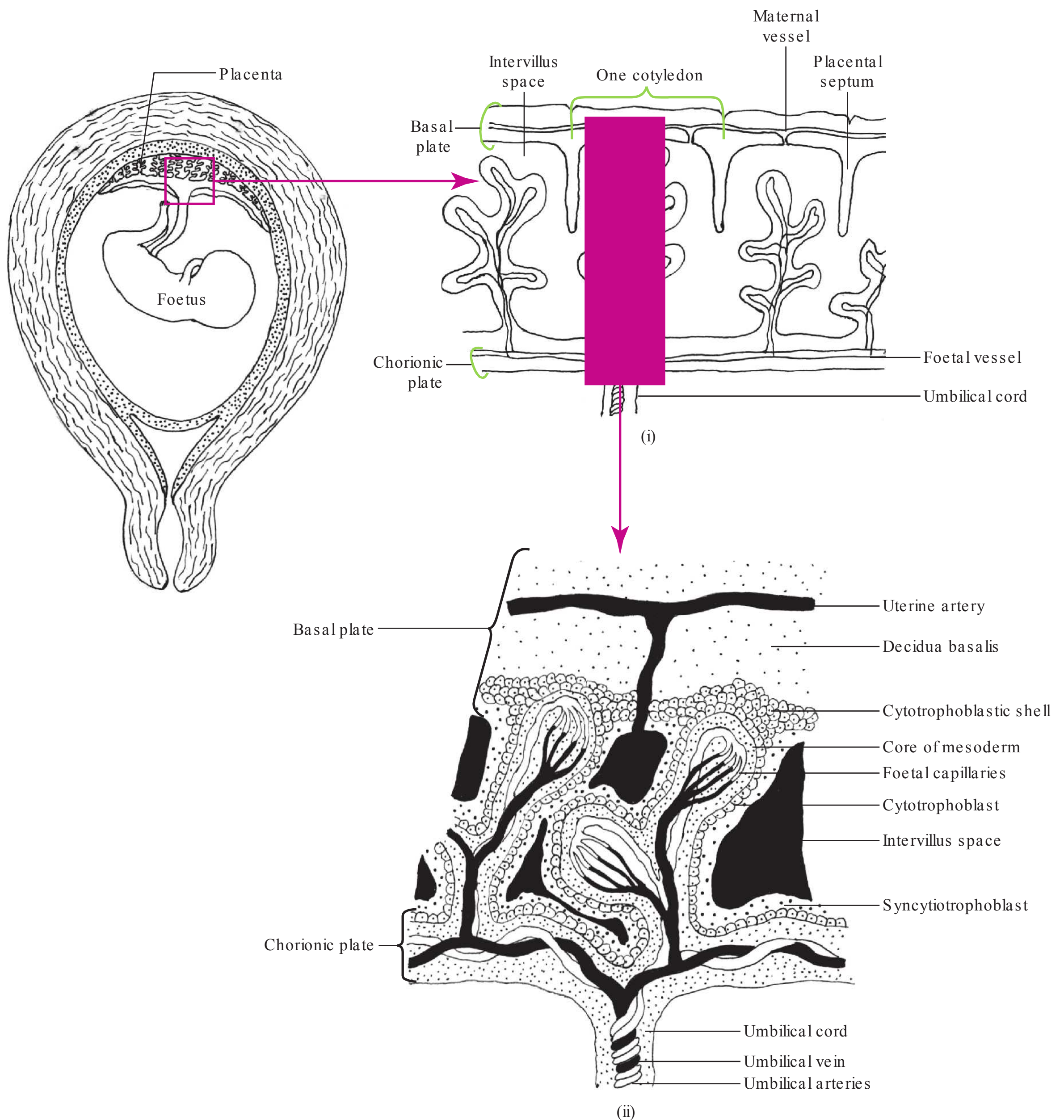
- Placenta is a disc-shaped organ with foetal and maternal surfaces.
- The foetal surface is covered by amnion and it is smooth. Umbilical cord is attached to this surface (Fig. 19.9).



**Figure 19.9** A full-term placenta.



- The maternal surface is irregular due to presence of cotyledons separated by placental septa (Fig. 19.9).
- The placenta consists of chorionic and basal plates. The chorionic plate is the foetal part. The basal plate consists of decidua basalis (maternal part) and cytotrophoblasts and syncytiotrophoblast (Fig. 19.10).



**Figure 19.10** Schematic diagram of mature placenta. In this figure, fetus connected to the placenta by umbilical cord can be seen. Inset (i) shows the maternal and foetal parts of placenta. Inset (ii) shows the villi connecting the maternal and foetal parts of placenta.

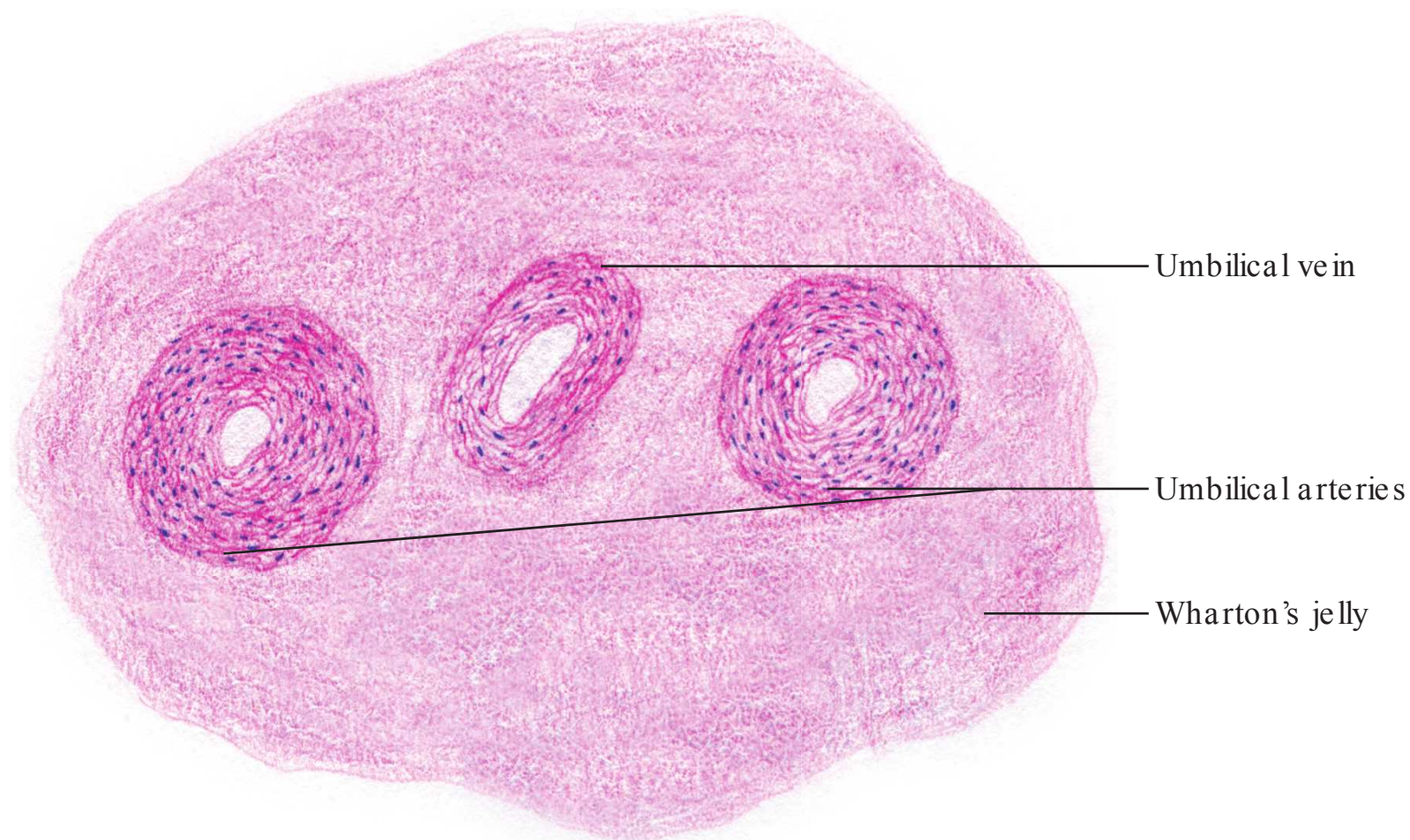


## PLACENTAL BARRIER

- It separates maternal blood from foetal blood.
- The nutrients from the maternal blood have to pass through a six-layered placental barrier: (a) syncytiotrophoblast, (b) cytotrophoblast, (c) basal lamina of cytotrophoblast, (d) loose connective tissue, (e) basal lamina of the blood vessel and (f) endothelium of the blood vessel.
- Some substances can pass through this barrier, and these substances can be beneficial (glucose, vitamins, amino acids, oxygen, carbon dioxide, water, etc.) or harmful (certain drugs—thalidomide, tetracycline, etc.; viruses—rubella, cytomegalovirus, etc.).

## UMBILICAL CORD

- It is formed by the primary mesoderm of the connective stalk surrounded by amnion.
- Inside the umbilical cord, there are two umbilical arteries and one umbilical vein (Fig. 19.11; PMG 19.2).



**Figure 19.11** Transverse section of umbilical cord in low magnification (H&E pencil drawing).



**PMG 19.2** Transverse section of placenta at term (H&E stain, X10).



- The primary mesoderm of the connective stalk is converted into Wharton's jelly; this tissue protects the umbilical vessels.
- Umbilical arteries convey deoxygenated blood from the foetus to the placenta, and umbilical vein conveys oxygenated blood from the placenta to the foetus.

## CLINICAL CORRELATES

### hCG

- hCG is a glycoprotein. Its concentration in maternal blood and urine is maximum during 8–10 weeks and then declines for the remainder of pregnancy. The presence of hCG in the maternal urine can be detected as early as 14 days after conception—this is the basis for one of the pregnancy tests.

### Foetoplacental Unit

- The synthesis of placental oestrogen occurs in syncytiotrophoblast. Its precursors are derived mainly from foetal adrenals. This is the basis for the foetoplacental unit; concentration of estriol in mothers' urine is monitored as an index of the state of the foetus.

## KEYPOINTS

### Placenta (Fig. 19.7; PMG 19.1)

- The placenta consists of the chorionic plate (foetal part) and basal plate (maternal part). The foetal and maternal parts of the placenta are connected by chorionic villi.

Parts	Components
Chorionic plate	From foetal to maternal side 1. Primary mesoderm with foetal blood vessels 2. Cytotrophoblast 3. Syncytiotrophoblast
Basal plate	From maternal to foetal side 1. Decidua basalis (maternal part) 2. Syncytiotrophoblast 3. Cytotrophoblast

### Umbilical Cord (Fig. 19.11; PMG 19.2)

- The transverse section of umbilical cord shows two umbilical arteries and one umbilical vein surrounded by Wharton's jelly.

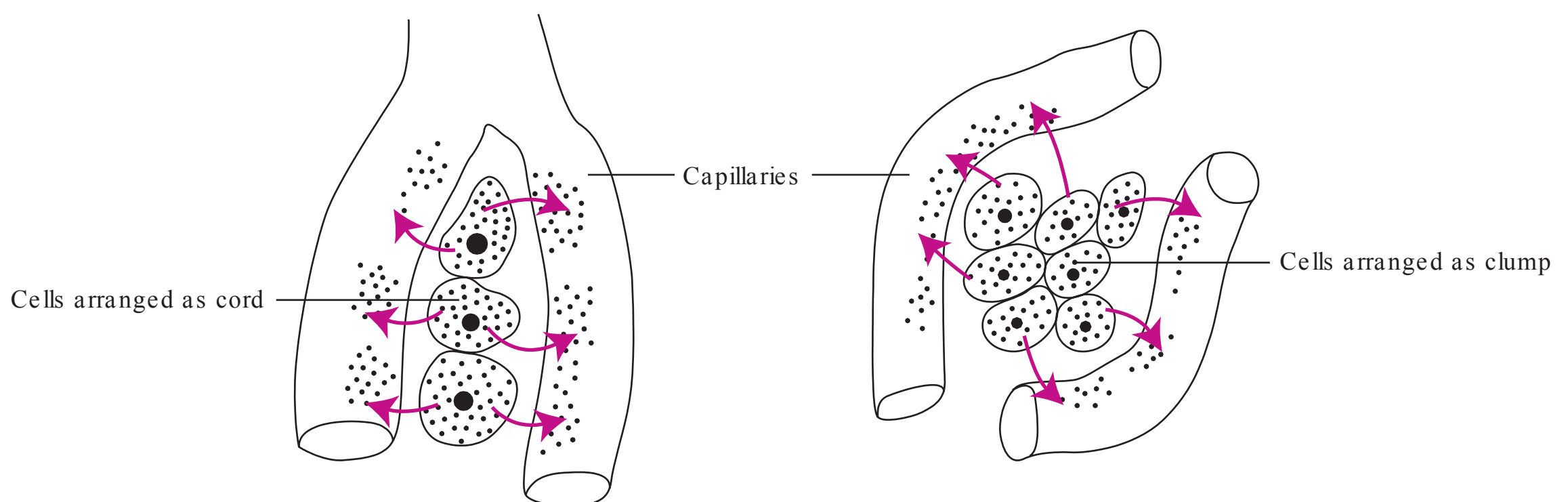
## SELF-ASSESSMENT

1. Describe the microscopic structure of placenta. Mention its functions.
2. Describe the microscopic structure of the umbilical cord.



# The Endocrine Glands

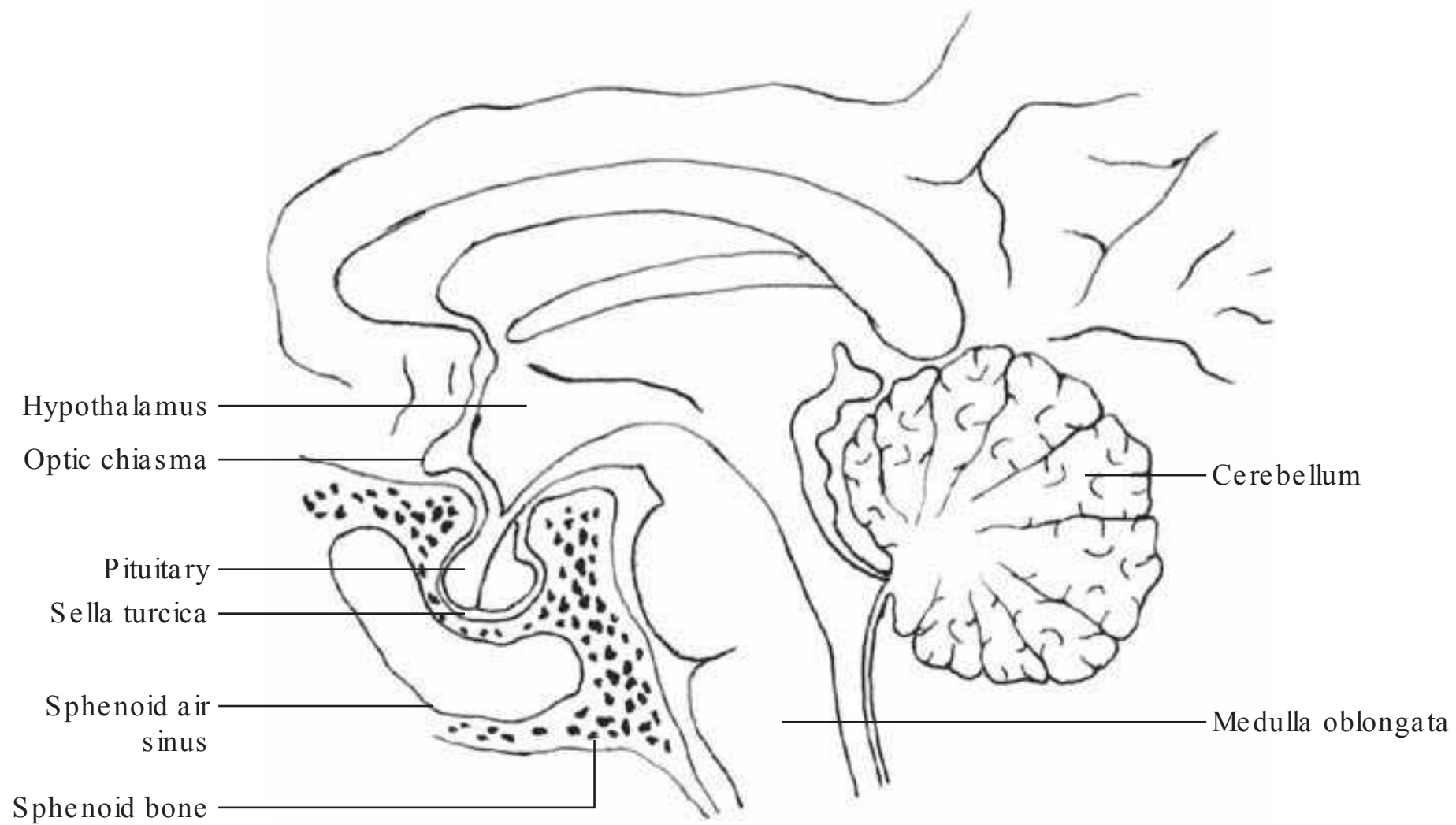
- The development of endocrine glands is discussed in Chapter 4. In this chapter, the histology of various endocrine glands is described.
- Endocrine glands are ductless glands. They develop as invaginations of surface epithelium; however they later get separated from the epithelium.
- The secretory cells of endocrine glands are arranged as cords or clumps around capillaries or sinusoids (Fig. 20.1). In some endocrine glands (such as thyroid), cells are arranged as follicles.
- Since these glands are ductless, the secretory cells release the hormones into the interstitial fluid. From the interstitial fluid, the hormones enter the bloodstream and reach their target organs.
- This chapter deals with pituitary, thyroid, parathyroid and adrenal glands. Other endocrine glands have been described in their respective systems.



**Figure 20.1** Arrangement of endocrine cells. The arrows show the secretions of endocrine cells entering the capillaries.

## PITUITARY GLAND

- The pituitary gland or the hypophysis is an endocrine gland; it is about the size of a pea.
- It is located in the base of the skull inside the bony cavity of the sphenoid bone, known as sella turcica (Fig. 20.2). It is connected to the hypothalamus by a pituitary stalk.
- The pituitary gland is considered the 'master gland' of the endocrine system as it secretes the hormones that regulate the other endocrine glands.



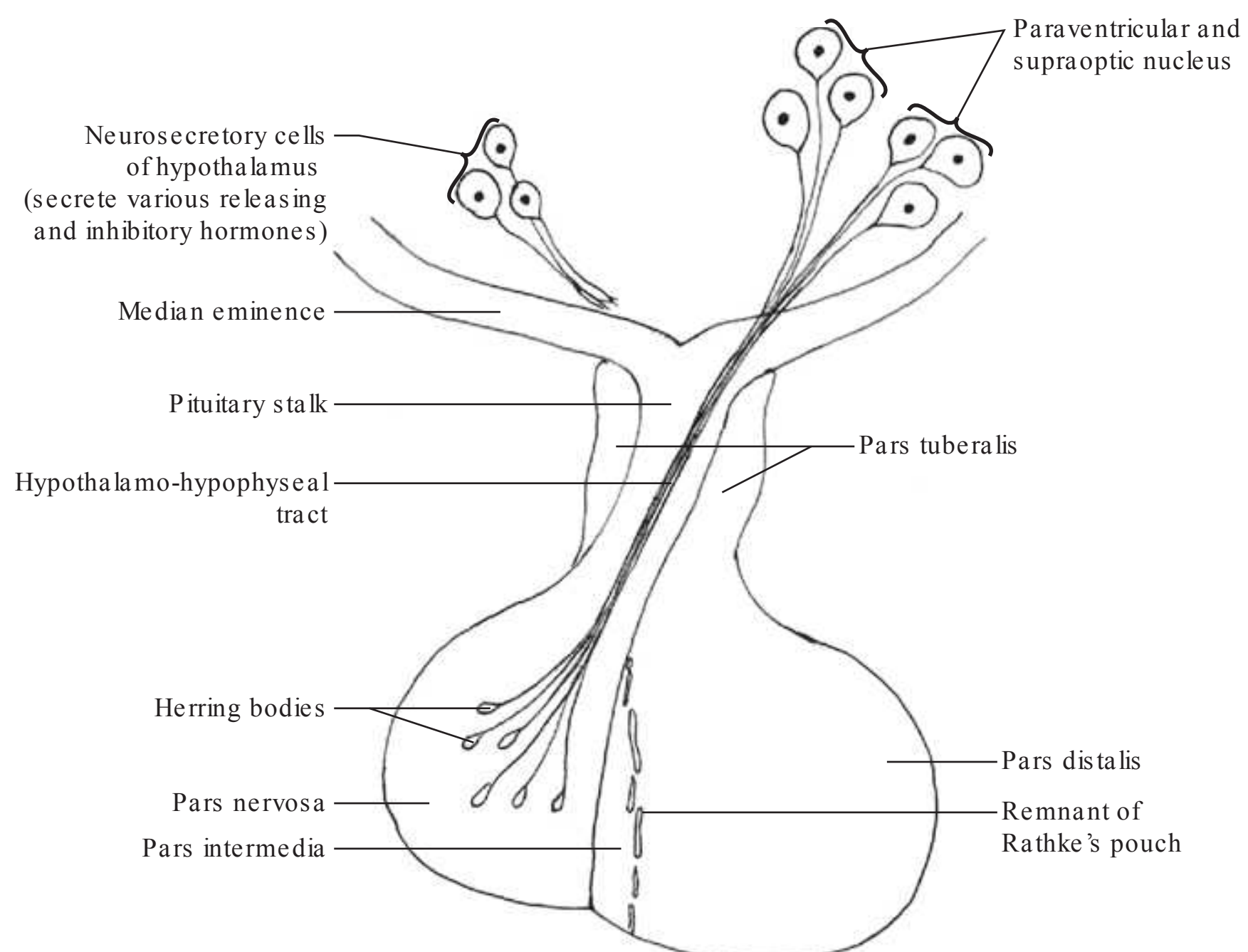
**Figure 20.2** Location of the pituitary gland inside the sella turcica at the base of skull (sagittal section).

### **PARTS OF PITUITARY** (Fig. 20.3; also see Fig. 20.5)

It consists of two parts: adenohypophysis and neurohypophysis.

#### **Adenohypophysis (Anterior Pituitary)**

- The anterior pituitary is further subdivided into following parts: pars distalis, pars tuberalis and pars intermedia.



**Figure 20.3** Parts of the pituitary gland. The hypothalamo-hypophyseal tract can also be seen.



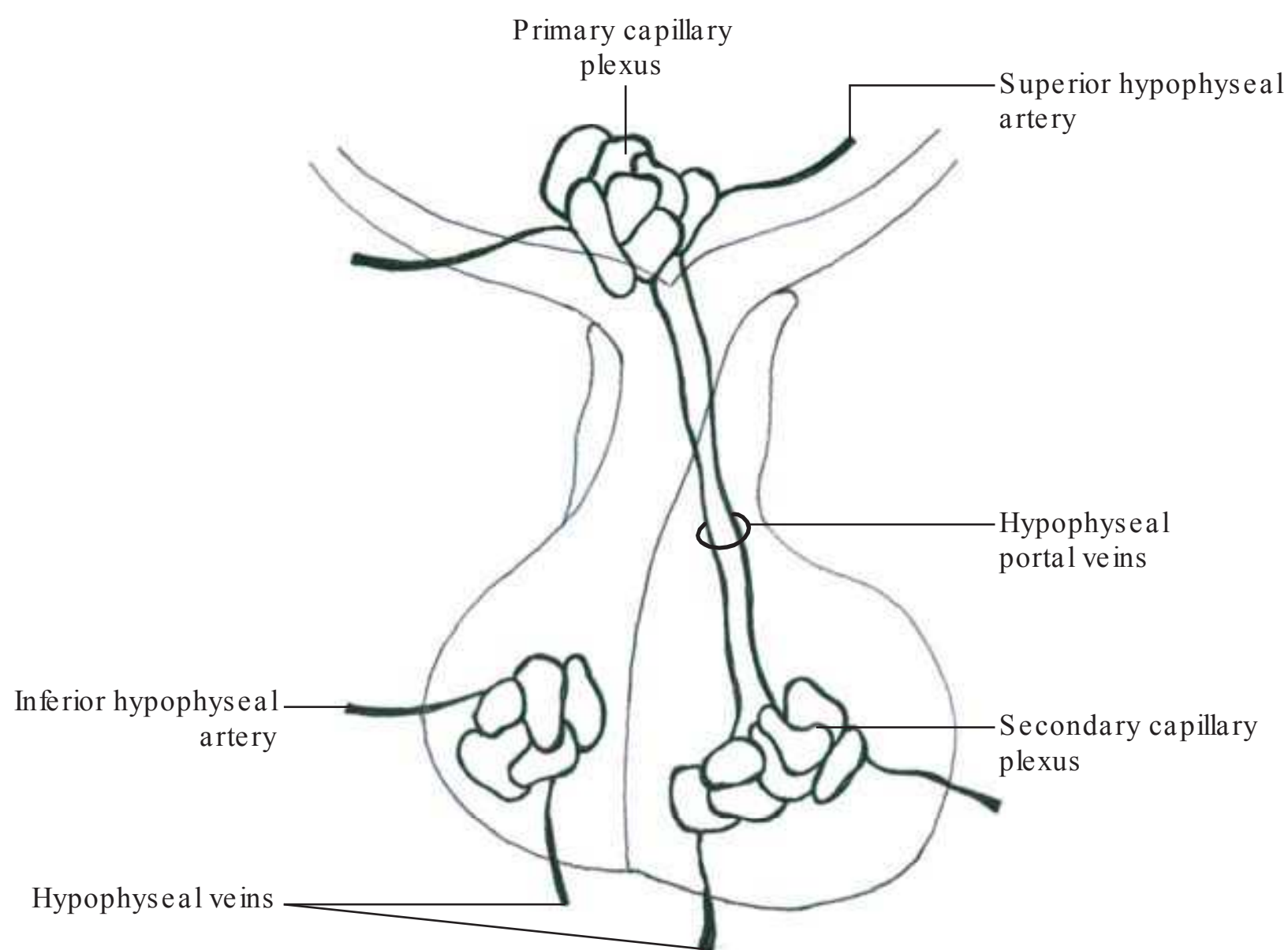
- Pars distalis or pars anterior is the largest part. Pars tuberalis is the upward extension of pars distalis surrounding the pituitary stalk. Pars intermedia is the part of adenohypophysis present as a thin band between the pars distalis and pars nervosa.
- Adenohypophysis develops from an outgrowth (Rathke's pouch) from the roof of the primitive oral cavity. The remnant of Rathke's pouch may persist as intraglandular cleft in anterior pituitary.

### Neurohypophysis (Posterior Pituitary)

- It develops from the downward growth of the hypothalamus.
- It consists of pars nervosa, infundibulum and median eminence.
- The major part of neurohypophysis is pars nervosa, which lies posterior to pars intermedia.
- Pars nervosa is connected to the hypothalamus by the pituitary stalk, also called infundibulum. Infundibulum is continuous with the median eminence.

### BLOOD SUPPLY (Fig. 20.4)

- The pituitary is supplied by superior and inferior hypophyseal arteries, which are branches of internal carotid arteries.
- The superior hypophyseal arteries form the primary capillary plexus in pars tuberalis, median eminence and infundibular stem and supply these parts. Blood from the primary capillary plexus drains into the secondary capillary plexus present in pars distalis, through hypophyseal portal veins. From the secondary capillary plexus, blood drains into hypophyseal veins. The secretions of the hypothalamus are transported from the median eminence to the adenohypophysis through hypophyseal portal veins (described in more detail under section 'Control of Anterior Pituitary Secretion' later in the chapter).
- Inferior hypophyseal arteries supply neurohypophysis.



**Figure 20.4** Blood supply of the pituitary gland.

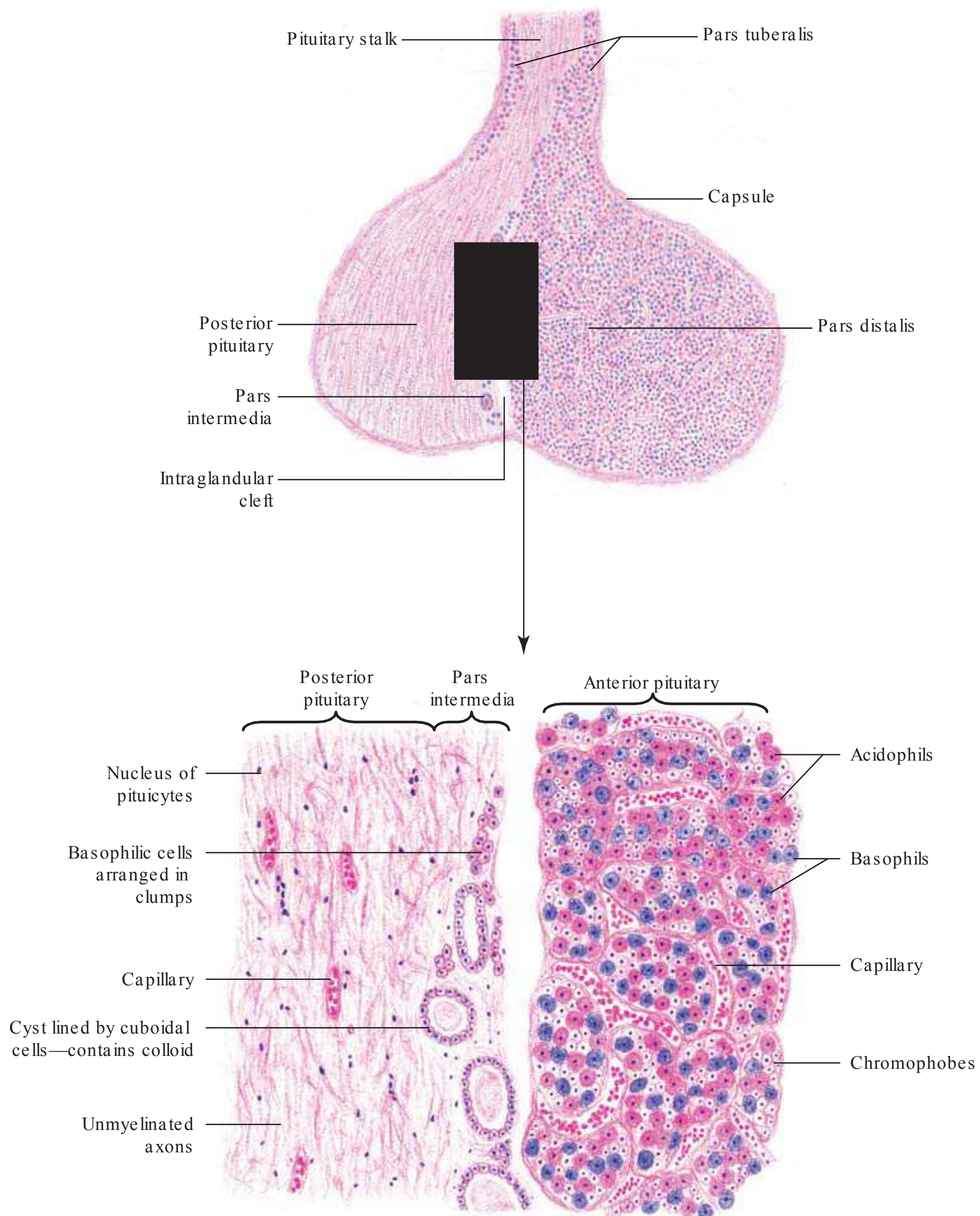
### MICROSCOPIC FEATURES

The entire gland is covered by a connective tissue capsule. The microscopic features of pars distalis, tuberalis and intermedia and neurohypophysis are as follows.



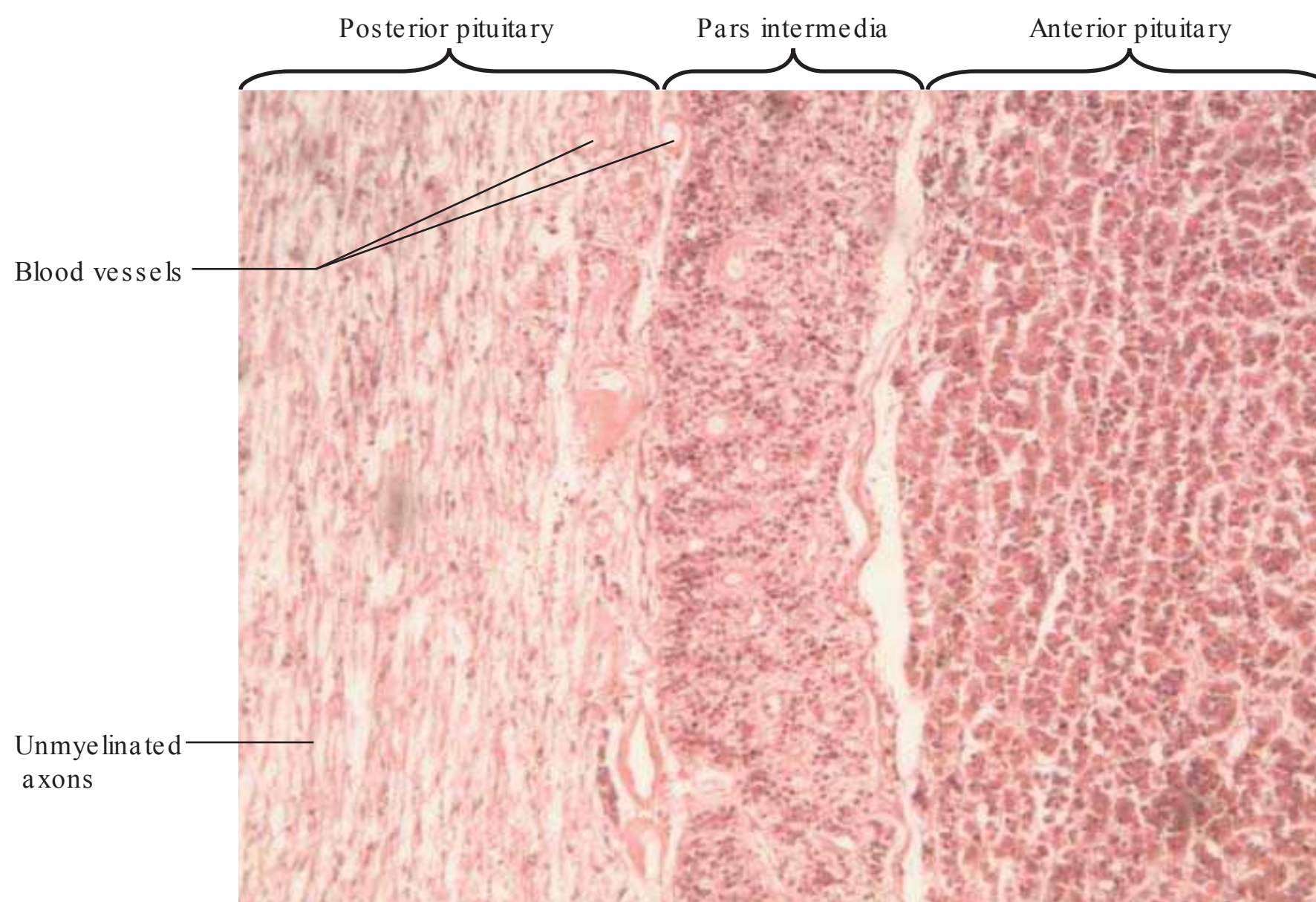
### Pars Distalis

- It consists of cells that are arranged in clumps or irregular cords between networks of capillaries (Fig. 20.5; PMG 20.1).
- These cells are supported by a network of reticular fibres.
- Based on their affinities for H&E stains, cells are classified as chromophobe and chromophil cells. Chromophil cells are further subdivided into acidophils and basophils.



**Figure 20.5** Panoramic view of pituitary gland. Inset shows section of gland in low magnification. (H&E pencil drawing)





**PMG 20.1** Pituitary gland (H&E stain, X10).

### *Acidophils*

- These cells stain well with acidic dyes (such as eosin and orange G) and are hence called acidophils.
- They are rounded cells (Fig. 20.5, inset), and their cytoplasm contains secretory granules.
- Based on their hormone products, acidophils are divided into two subtypes: somatotrophs and mam-motrophs. Somatotrophs produce growth hormone (GH) and mammotrophs produce prolactin.

### *Basophils*

- These cells stain well with haematoxylin and periodic acid–Schif.
- They are polygonal in shape (Fig. 20.5, inset), and their cytoplasm contains secretory granules.
- Based on hormones produced by them, the basophils are divided into three subtypes: thyrotrophs, gonadotrophs and corticotrophs.
- Thyrotrophs produce thyroid-stimulating hormone (TSH), gonadotrophs produce follicle-stimulating hormone (FSH) and luteinising hormone (LH), and corticotrophs produce adrenocorticotrophic hormone (ACTH).

### *Chromophobes*

- They are the smallest cells (Fig. 20.5, inset) and are present in clusters.
- These cells are poorly stained and contain very few cytoplasmic granules.

### **Pars Tuberalis**

- It is same as pars distalis.

### **Pars Intermedia**

- Small cysts containing colloid, lined by cuboidal cells, can also be seen, and these cysts are remnants of Rathke's pouch.
- It contains basophilic cells arranged in irregular clumps and cords (Fig. 20.5, inset; PMG 20.1).
- The cells of pars intermedia produce melanocyte-stimulating hormone (MSH).

### Neurohypophysis (Posterior Pituitary)

- Neurohypophysis stores the hormones synthesised in the hypothalamus.
- It contains the hypothalamo-hypophyseal tract, which consists of unmyelinated axons of neurosecretory cells (Figs 20.3 and 20.5). The cell bodies of these neurons are located in supraoptic and paraventricular hypothalamic nuclei of the hypothalamus.
- It also contains supporting cells called pituicytes (Fig. 20.5).
- Neurosecretory products (oxytocin and vasopressin) are produced by the cell bodies of the neurosecretory cells, in the hypothalamus. Two hormones, oxytocin and antidiuretic hormone (ADH) or vasopressin, pass through the axons of the hypothalamo-hypophyseal tract to the posterior pituitary (Fig. 20.3) where they are contained in axonal swellings called Herring bodies (Fig. 20.3). The products are finally released into the capillaries.

### PITUITARY HORMONES

The pituitary, the master gland of the endocrine system, produces several hormones which have vast effects on various systems of the body (Table 20.1).

**Table 20.1** Major Pituitary Hormones and Their Physiological Effects

Part of pituitary	Type of cell	Hormones	Target	Effects
Anterior pituitary	Somatotropes (acidophils)	GH	Cells of epiphyseal cartilage and most of the other cells in the body	Growth of long bones Increased growth rate
	Mammotropes (acidophils)	Prolactin	Alveolar cells of mammary gland	Development of mammary gland during pregnancy and milk production during lactation
	Thyrotropes (basophils)	TSH	Follicular cells of thyroid	Promotion of synthesis and secretion of $T_3$ and $T_4$
	Gonadotropes (basophils)	FSH	Follicular cells of ovary	Promotion of growth of ovarian follicle
			Sertoli cells of testes	Production of androgen-binding protein which stimulates spermatogenesis
		LH	Ovarian follicles and corpus luteum	Ovulation and progesterone synthesis
			Leydig cells of testes	Testosterone synthesis and secretion
	Corticotropes (basophils)	ACTH	Zona fasciculata (adrenal cortex)	Promotion of glucocorticoid secretion
			Zona reticularis (adrenal cortex)	Promotion of adrenal androgen secretion
Posterior pituitary	Cell bodies of neurosecretory nerve cells in supraoptic and paraventricular hypothalamic nuclei	ADH	Collecting tubules and ducts of kidney	Concentration of urine due to resorption of water
		Oxytocin	Myoepithelial cells of mammary gland	Milk ejection
			Smooth muscles of uterus	Contraction during copulation and parturition

ACTH, adrenocorticotrophic hormone; ADH, antidiuretic hormone; FSH, follicle-stimulating hormone; GH, growth hormone; LH, luteinising hormone; TSH, thyroid-stimulating hormone.



### Anterior Pituitary Hormones (Table 20.1)

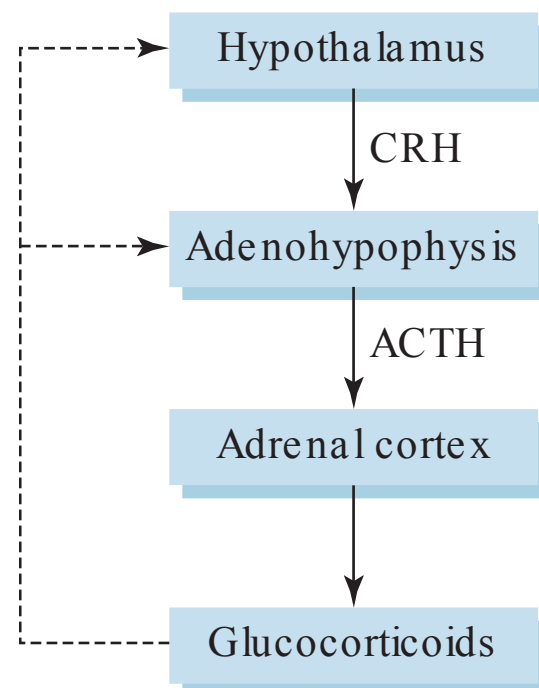
1. **Growth hormone (GH):** Somatotrophs produce growth hormone, which is important for body growth and development in children and adolescents. It stimulates production of somatomedin in the liver, and somatomedin then acts on epiphyseal cartilage and causes growth of long bones. In most of the cells in the body, it increases the rate of metabolism.
2. **Prolactin:** Mammotrophs produce prolactin, which promotes mammary gland development during pregnancy and maintains milk secretion during lactation.
3. **Thyroid-stimulating hormone (TSH):** Secreted by thyrotrophs, it acts on follicular cells of thyroid and stimulates synthesis and release of thyroid hormones.
4. **Follicle-stimulating hormone (FSH):** Produced by gonadotrophs, it stimulates growth of ovarian follicles and secretion of oestrogen in females. In males, it acts on Sertoli cells of the seminiferous tubules, which synthesise androgen-binding protein, and this protein stimulates spermatogenesis.
5. **Luteinising hormone (LH):** Produced by gonadotrophs, it induces ovulation, formation of corpus luteum and secretion of progesterone in females. In males, it stimulates production of testosterone by the interstitial cells of the testis.
6. **Adrenocorticotrophic hormone (ACTH):** Produced by corticotrophs, it stimulates synthesis and secretion of glucocorticoids in zona fasciculata and adrenal androgen in zona reticularis of the adrenal cortex.

### Posterior Pituitary Hormones (Table 20.1)

1. **Oxytocin:** It is released in lactating women. The release of oxytocin is caused by a neuronal reflex that is initiated during suckling. Oxytocin causes contraction of myoepithelial cells around the secretory alveoli of the mammary gland and causes ejection of milk. Oxytocin causes contraction of smooth muscles in the uterus and fallopian tube during copulation and facilitates sperm transport. Oxytocin also induces contraction of uterine smooth muscles during parturition.
2. **Antidiuretic hormone (ADH):** It helps in resorption of water in the kidney to produce concentrated urine. It increases the permeability of collecting tubules of the kidney to water, which results in concentration of urine and a decrease in its volume. In diabetes insipidus there is deficiency of ADH, the urine becomes hypotonic to plasma, and the urine volume is increased—all of these result in water loss.

### Control of Anterior Pituitary Secretion

- The adenohypophysis, which controls various endocrine organs, is itself under the control of the hypothalamus.
- The neurosecretory cells of the hypothalamus secrete various stimulating and inhibitory hormones. The axons of these neurosecretory cells terminate in median eminence and release the hormones (Fig. 20.3). The hormones are transported from the median eminence to the adenohypophysis through hypophyseal portal veins (Fig. 20.4) and stimulate or inhibit the acidophils and basophils.
- The secretions of neurosecretory cells of hypothalamus are regulated by the level of hormones, by negative feedback mechanism. For example, the hypothalamus secretes corticotropin-releasing hormone (CRH), which stimulates corticotrophs of adenohypophysis to synthesise and secrete ACTH, which in turn stimulates the adrenal cortex to synthesise and secrete glucocorticoids (Fig. 20.6). Once glucocorticoids have been released into the blood in sufficient amount, they inhibit the hypothalamus from releasing CRH and the adenohypophysis from releasing ACTH, through negative feedback mechanism (Fig. 20.6).



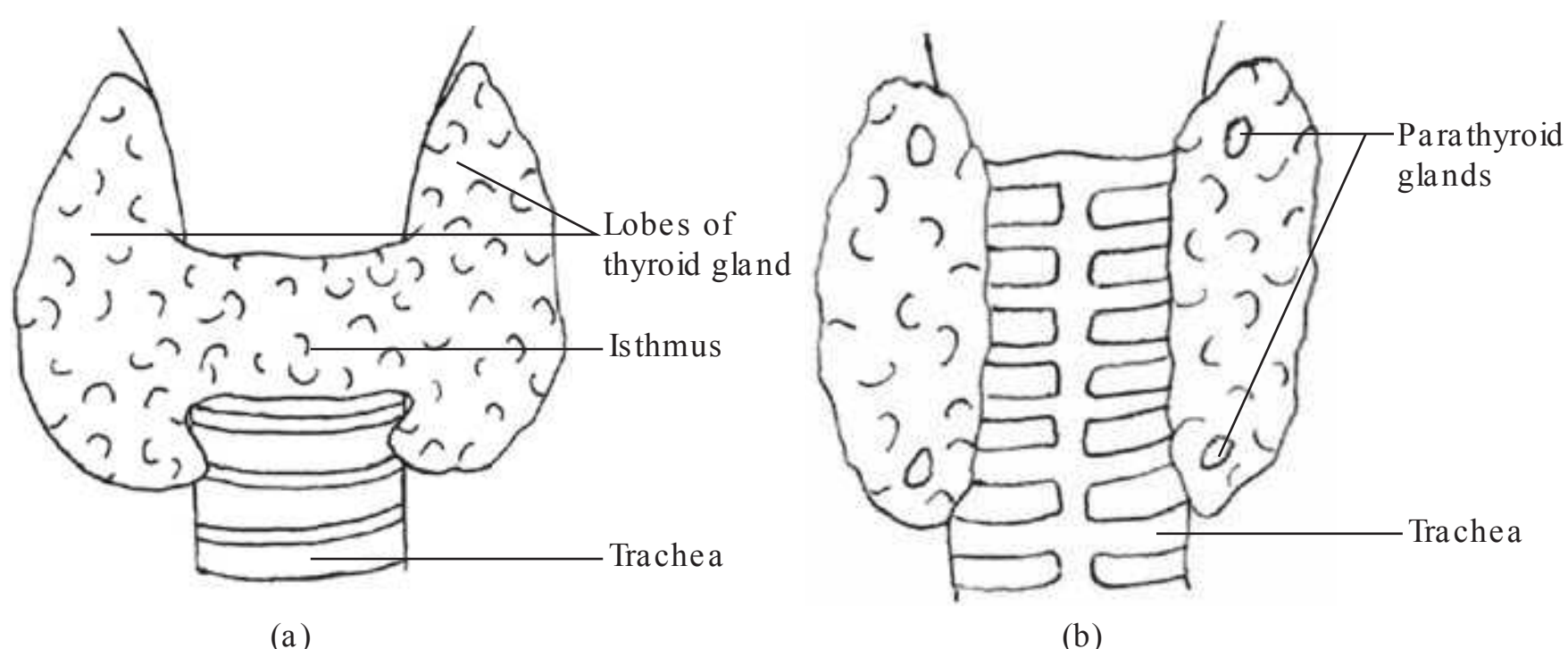
**Figure 20.6** Negative feedback mechanism of glucocorticoids. The solid arrows indicate stimulatory effects and dashed arrows indicate inhibitory effects. ACTH, adrenocorticotrophic hormone; CRH, corticotropin-releasing hormone.

### Control of Posterior Pituitary Secretion

- ADH is stored in the Herring bodies of the secretory neurons in posterior pituitary, and it is released into the blood by the impulses in these neurons.
- Increase in plasma osmolality or a decrease in blood volume (or blood pressure) triggers the release of ADH into the blood.
- Like ADH, oxytocin is also stored in the Herring bodies. The release of oxytocin is triggered by neuroendocrine reflex, which is initiated by stimulation of touch receptors present on the nipple, while suckling.

## THYROID GLAND

The thyroid is a bilobed organ, located in the anterior aspect of the neck (Fig. 20.7). The two lobes are connected to each other by the isthmus in front of the trachea.

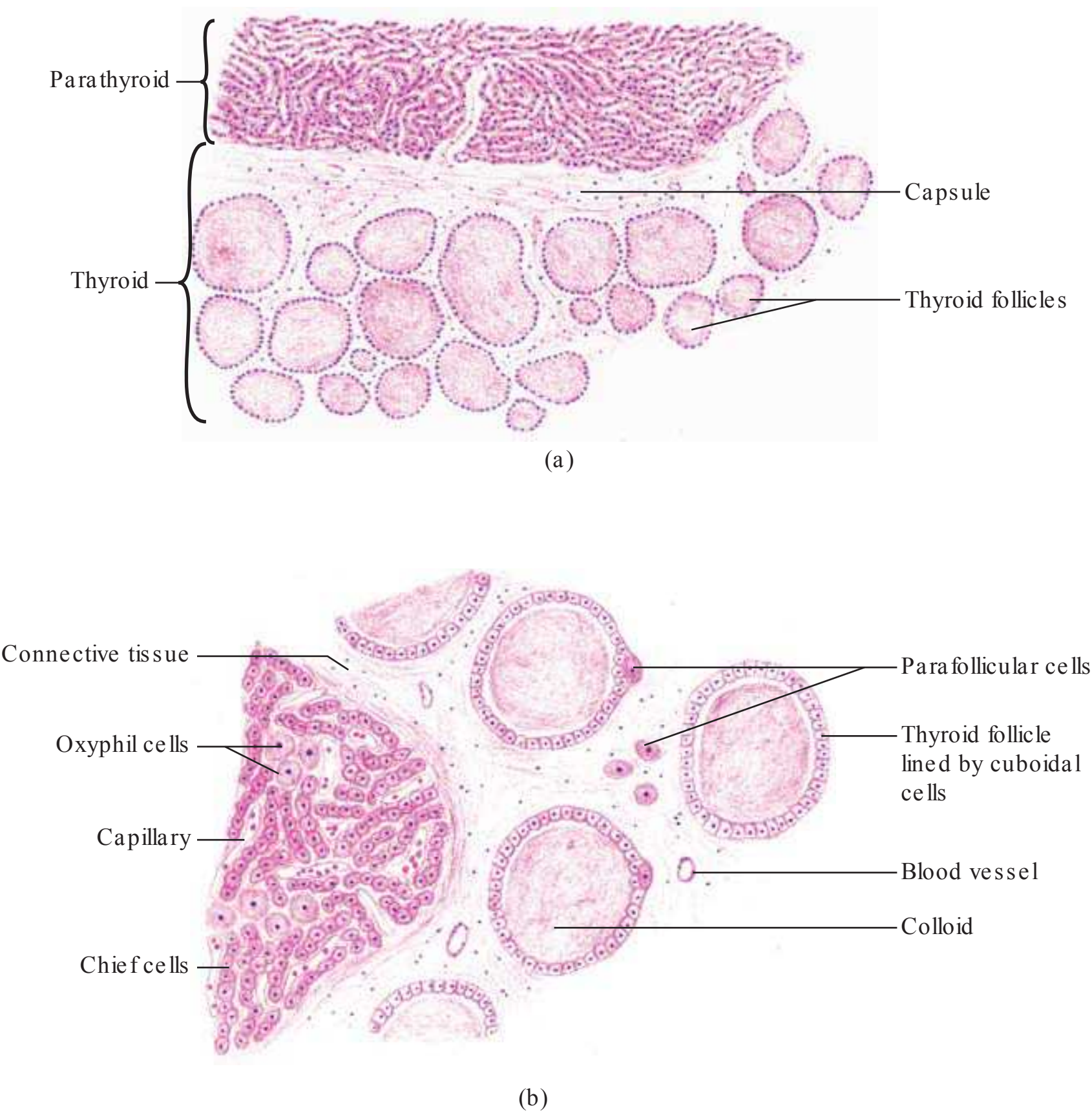


**Figure 20.7** Diagram of thyroid gland: (a) anterior view showing the parts of thyroid gland and (b) posterior view showing the location of parathyroid glands.

### MICROSCOPIC FEATURES (Fig. 20.8; PMG 20.2)

- It is covered by a thin connective tissue capsule. Many septa arise from the capsule, and they convey blood vessels, nerves and lymphatics into the gland.
- The parenchyma consists of hollow, spheroidal structures called thyroid follicles and parafollicular cells.





**Figure 20.8** Section of thyroid and parathyroid glands in (a) low and (b) high magnification (H&E pencil drawing).



**PMG20.2** Thyroid and parathyroid glands (H&Estain, X10).

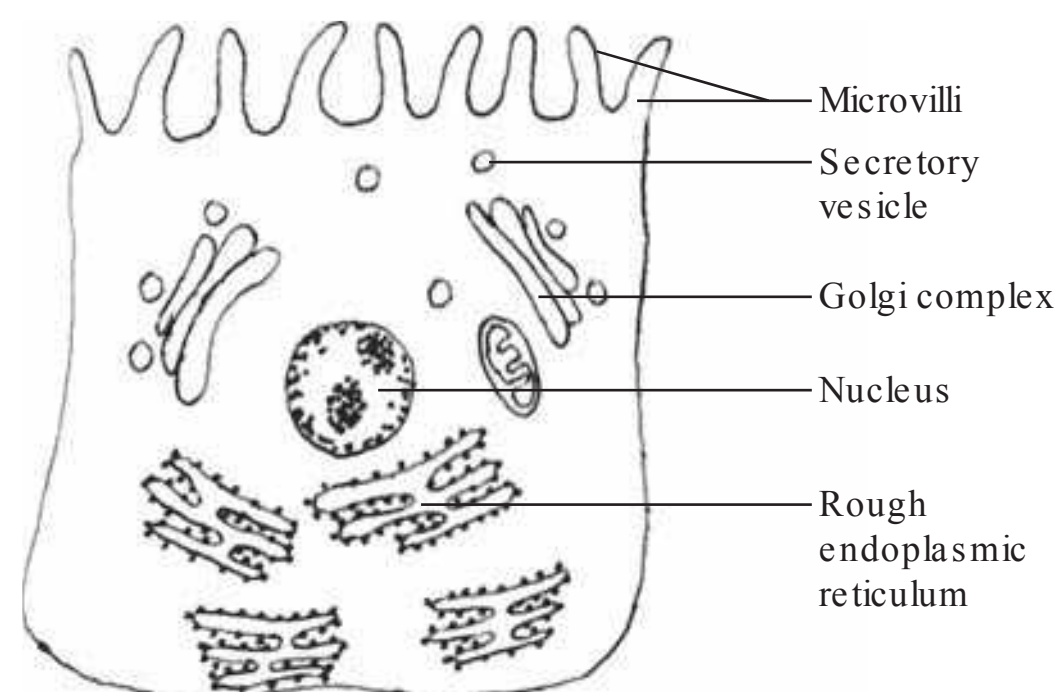


## Thyroid Follicle

- The wall of thyroid follicle consists of a single layer of cells called follicular cells. These cells rest on a basement membrane.
- The connective tissue between the follicles contains capillaries, nerves and lymphatic vessels.
- The lumen of the follicle is filled with a colloid material.
- Follicular cells are usually cuboidal, but the shape varies depending upon the functional status of the follicles. In actively secreting follicles, the amount of colloid decreases and the cells lining the follicle become tall. In less active follicles, the amount of colloid is more and lining cells become flat.
- The colloid is formed by the follicular cell. Its main component is thyroglobulin, which is the inactive storage form of thyroid hormone.
- Thyroid is unique among endocrine glands as it stores its secretory product, colloid, extracellularly in the lumen of the follicle.

### Follicular Cells (Fig. 20.9)

- Each follicular cell has a spherical nucleus containing one or two nucleoli.
- The lateral plasma membranes have junctional complexes towards the apex.
- The luminal surface of follicular cells has microvilli.
- The basal cytoplasm has numerous rough endoplasmic reticulum. Golgi complexes and numerous colloid resorption droplets are present in apical cytoplasm.



**Figure 20.9** Follicular cell.

## Parafollicular Cells

- These cells are also called 'C' cells.
- They are present in clusters in the connective tissue in between the follicles. They are also present as single cells within the follicle (Fig. 20.8b). Within the follicle, they are located away from the colloid, adjacent to the basement membrane.
- They secrete calcitonin hormone which reduces the blood calcium level by reducing bone resorption by osteoclasts.

## HORMONES OF THYROID GLAND

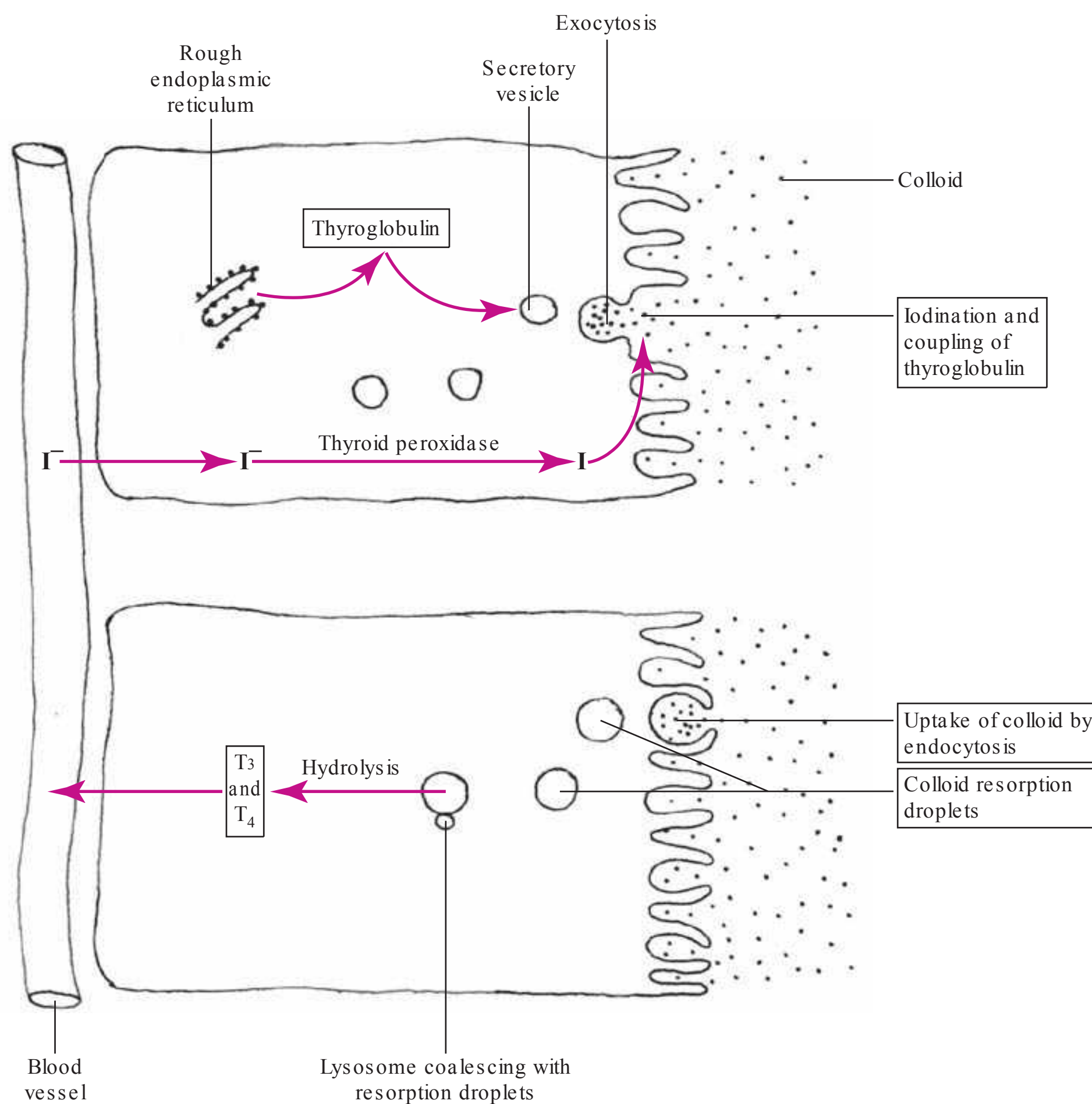
- Thyroid hormone increases the basal metabolic rate in most of the tissues. It is essential for normal body growth and development of the central nervous system.
- Calcitonin antagonises the action of parathyroid hormone by reducing the blood calcium levels and thus helps to maintain the blood calcium level.



**Synthesis of Thyroid Hormone** (Fig. 20.10)

Thyroid hormone synthesis involves the following steps:

- 1. Synthesis and storage:** Thyroglobulin is synthesised by rough endoplasmic reticulum and is then carried to Golgi complex, where it is packed into vesicles. These vesicles are transported to the apical surface of the cell where thyroglobulin is discharged into the lumen of the follicle by exocytosis.

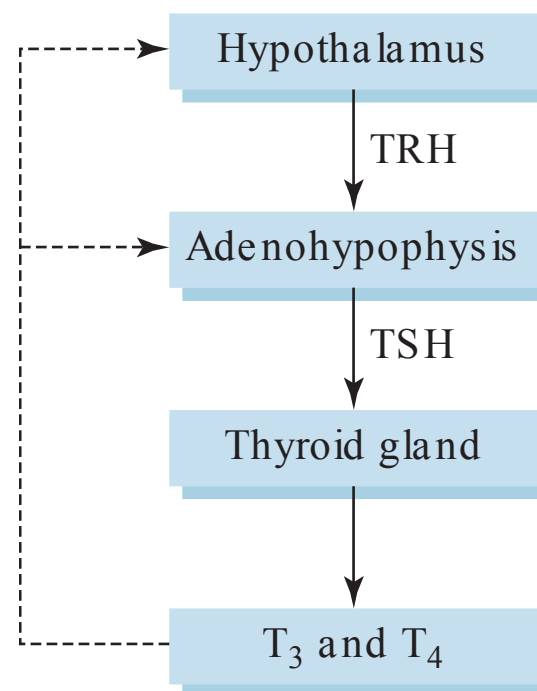


**Figure 20.10** Steps of thyroid hormone synthesis.

- 2. Iodide uptake:** Under the influence of TSH, follicular cells take up iodine from the blood. Iodide is oxidised to iodine by enzyme thyroid peroxidase.
- 3. Iodination of thyroglobulin:** Iodination of thyroglobulin occurs at the luminal surface of the follicular cells. Triiodothyronine ( $T_3$ ) and tetraiodothyronine ( $T_4$ , also known as thyroxine) are formed.
- 4. Release of thyroid hormones:** Stimulation of follicular cells by TSH causes endocytosis of thyroglobulin. Numerous colloid resorption droplets containing iodinated thyroglobulin are formed. Lysosomes fuse with the colloid resorption droplets and release  $T_4$  and  $T_3$  hormones, which enter blood circulation.

### Control of Thyroid Hormone

- Secretion of thyroid hormone is under the control of TSH, produced by adenohypophysis, through negative feedback mechanism (Fig. 20.11).
- The hypothalamus secretes thyrotropin-releasing hormone (TRH), which stimulates thyrotrophs of adenohypophysis to synthesise and secrete TSH, which in turn stimulates the follicular cells of thyroid to synthesise and secrete  $T_3$  and  $T_4$ . Once  $T_3$  and  $T_4$  have been released into the blood in sufficient amount, they inhibit the hypothalamus from releasing TRH and the adenohypophysis from releasing TSH, through negative feedback mechanism.



**Figure 20.11** Negative feedback mechanism of thyroid hormones. Solid arrows indicate stimulatory effects and dashed arrows indicate inhibitory effects. TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone.

## PARATHYROID GLANDS

There are two pairs of parathyroid glands. They are embedded in the capsule of thyroid on its posterior aspect (Fig. 20.7).

### MICROSCOPIC FEATURES (Fig. 20.8; PMG 20.2)

Parathyroid glands contain two types of cells: principal or chief cells and oxyphil cells.

#### Chief Cells

- Chief cells are the most numerous cells; they are polygonal in shape and are arranged in clumps or irregular cords.
- The cytoplasm of the cells shows numerous secretory granules; each cell has a centrally located spherical nucleus.
- Large capillaries are present in between the cords and clumps.
- Chief cells secrete parathyroid hormone (PTH or parathormone).

#### Oxyphil Cells

- These cells are larger in size but fewer in number than chief cells.
- They are arranged in clumps.
- Their function is not clear.

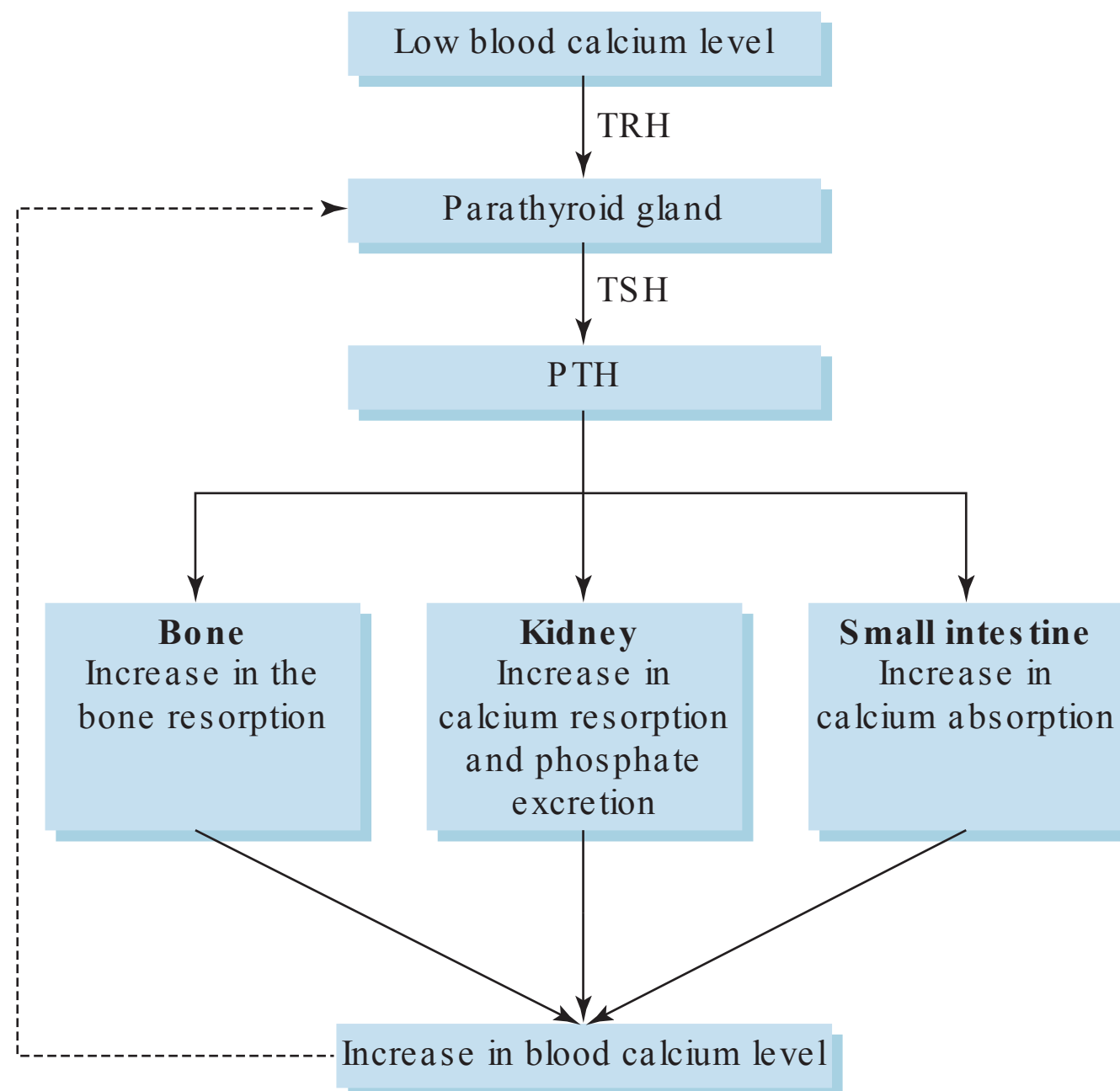
### PARATHYROID HORMONE

- PTH is secreted by the chief cells. It raises the blood calcium level.
- PTH acts on three different sites to increase the blood calcium level: bone, kidney and intestine (Fig. 20.12). In the bone, PTH acts on osteoclasts and increases the bone resorption. In kidney, PTH decreases phosphate resorption in proximal tubules and increases calcium resorption in distal tubules. PTH increases the absorption of calcium in the small intestine.



### Control of Parathyroid Secretion

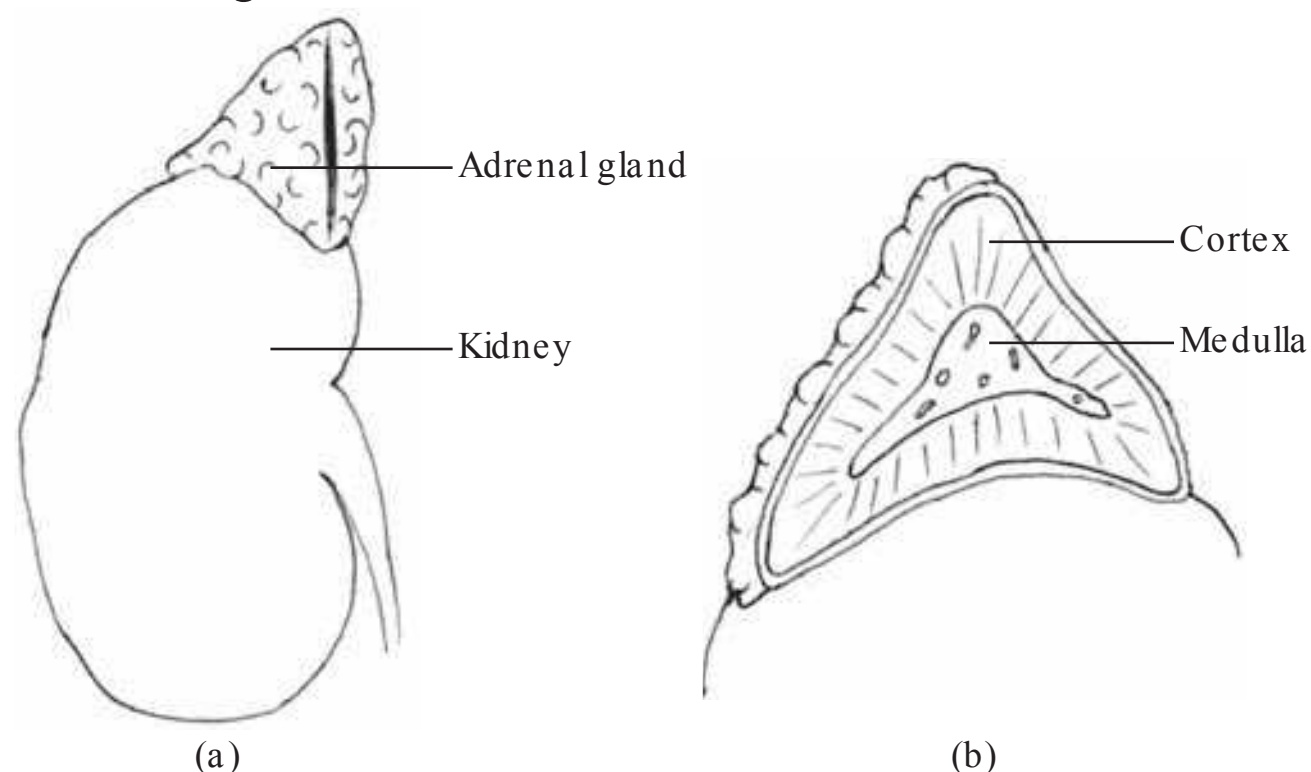
- The secretion of the parathyroid is regulated by the calcium level in blood, by negative feedback mechanism (Fig. 20.12).
- The low blood calcium level stimulates the gland to produce and secrete PTH. As described in the preceding text, PTH acts on kidney, bone and small intestine and increases the blood calcium level.
- Increase in the blood calcium level inhibits the parathyroid gland.



**Figure 20.12** Negative feedback mechanism of parathyroid hormone. Solid arrows indicate stimulatory effects and dashed arrow indicates inhibitory effects. PTH, parathyroid hormone; TRH, thyrotropin-releasing hormone; TSH, thyroid-stimulating hormone.

## ADRENAL GLANDS

- An adrenal gland is located at the upper pole of each kidney (Fig. 20.13).
- Each gland has two components: cortex and medulla (Fig. 20.13). Both components have different structural organisation, origin and functions.

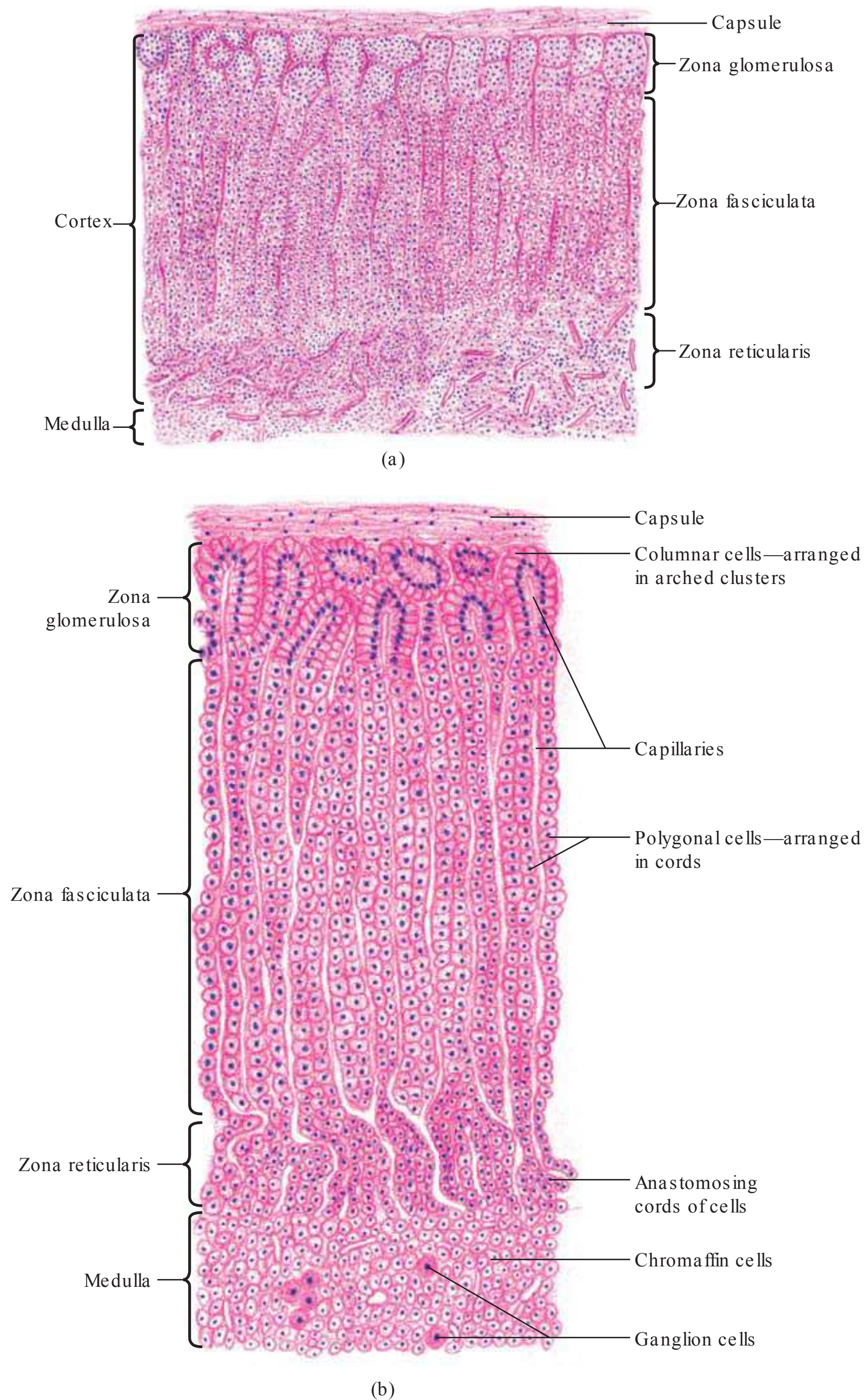


**Figure 20.13** Adrenal gland: (a) location and (b) its two components.



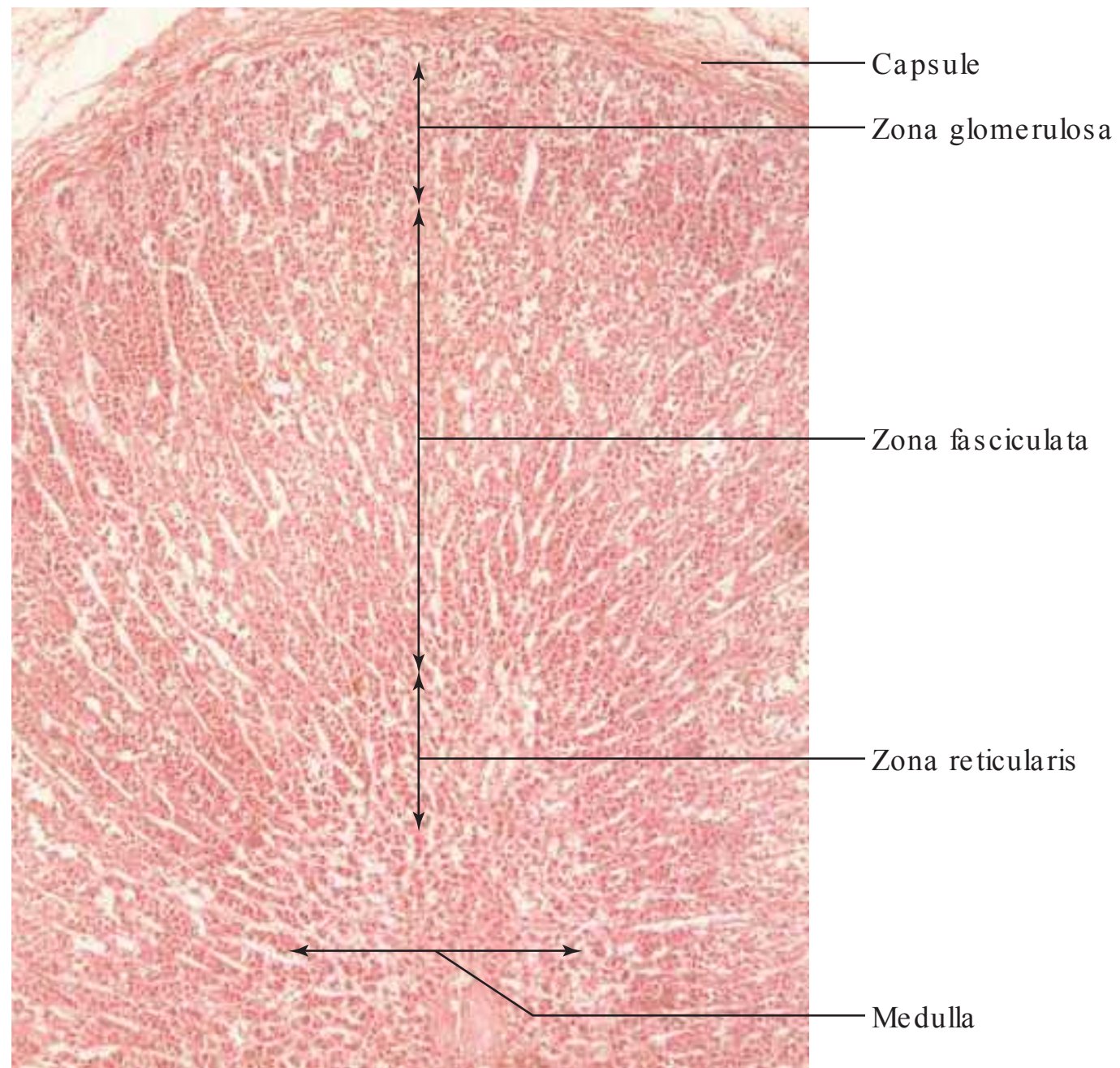
**MICROSCOPIC FEATURES** (Fig. 20.14; PMG 20.3)

- As mentioned earlier, the adrenal gland consists of two components: outer cortex and inner medulla (Fig. 20.14).
- Each gland is enclosed in a connective tissue capsule. Connective tissue septa extend from the capsule towards the medulla, conveying the vessels and nerves.

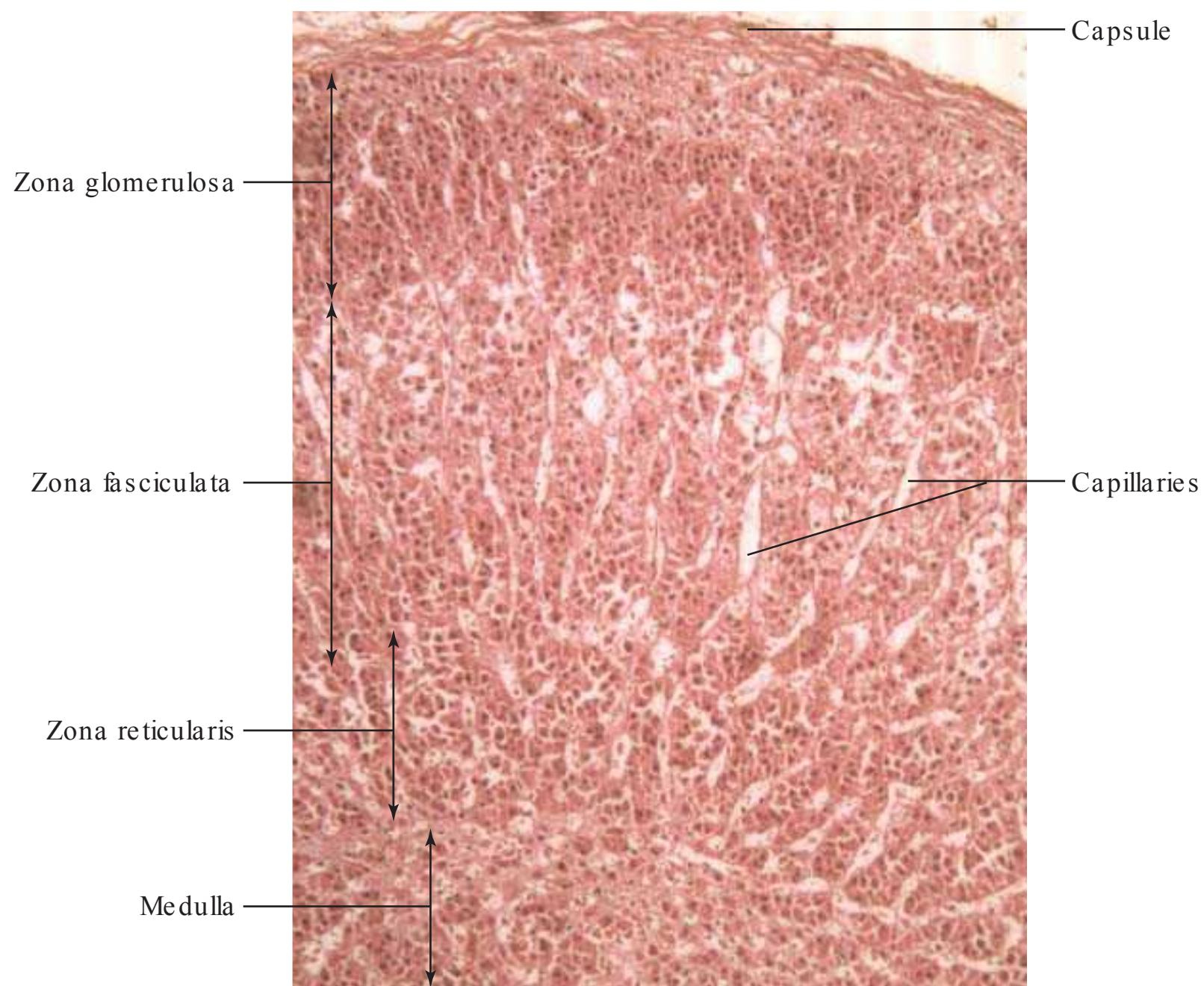


**Figure 20.14** Section of adrenal gland in (a) low and (b) high magnification (H&E pencil drawing).





(a)



(b)

**PMG 20.3** Adrenal gland: (a) X5 and (b) X10 (H&E stain).

### Adrenal Cortex

- It develops from mesoderm.
- It consists of three layers: outermost zona glomerulosa, middle zona fasciculata and innermost zona reticularis (Fig. 20.14).



*Zona Glomerulosa*

- It lies underneath the capsule (Fig. 20.14; PMG 20.3).
- It consists of columnar cells arranged in arch-shaped clusters, separated by thin connective tissue and capillaries. These cells have spherical nuclei.
- Cells of zona glomerulosa secrete mineralocorticoids such as aldosterone.

*Zona Fasciculata*

- Beneath the zona glomerulosa, there is a thick layer called zona fasciculata.
- Cells are arranged in one (or two) cell thick straight cords (Fig. 20.14; PMG 20.3). Cords are parallel to each other, separated by thin connective tissue and capillaries.
- Cells are large in size and polygonal in shape; each cell has a single, centrally placed, spherical nucleus.
- The cytoplasm of cells of zona fasciculata has numerous lipid droplets. During histological preparation, the lipid is lost, and the cytoplasm appears vacuolated. Hence, these cells are also called spongiocytes.
- The cells of zona fasciculata secrete glucocorticoids such as cortisol.

*Zona Reticularis*

- It is a relatively thin layer.
- It consists of polygonal cells, arranged in irregular anastomosing cords, separated by thin connective tissue and capillaries (Fig. 20.14; PMG 20.3).
- Cells are smaller in size than those of the zona fasciculata.
- Cells of zona reticularis secrete the steroid sex hormone adrenal androgen.

**Adrenal Medulla**

- It develops from neural crest cells.
- It consists of two types of cells: chromaffin cells and ganglion cells.

*Chromaffin Cells*

- They are the most numerous cells in the adrenal medulla.
- They are ovoid-shaped secretory cells, arranged in clumps or cords surrounding the capillaries (Fig. 20.14b).
- The cytoplasm of these cells has secretory granules containing catecholamines (adrenaline and nor-adrenalin). These secretory granules stain with stains containing chromium salts (chromaffin reaction), and hence these cells are called chromaffin cells.
- Chromaffin cells are innervated by preganglionic sympathetic fibres, and they correspond functionally to postganglionic sympathetic neurons as both are derived from neural crest cells.

*Ganglion Cells*

- In addition to the chromaffin cells, the medulla also contains a few sympathetic ganglion cells, singly or in small groups (Fig. 20.14b).
- They are larger in size than chromaffin cells.

**ADRENAL HORMONES**

- Adrenal cortex secretes three hormones: mineralocorticoids (aldosterone), glucocorticoids and adrenal androgens. Adrenal medulla secretes catecholamines.
  - (a) Aldosterone: It is secreted from zona glomerulosa of adrenal cortex. It regulates the resorption of sodium and excretion of potassium in the tubules of the kidney.
  - (b) Glucocorticoids: Glucocorticoids are secreted from zona fasciculata. They have various effects on protein, fat and glucose metabolism. They increase the blood glucose level. They also decrease the cellular and humoral immunity.
  - (c) Adrenal androgen: Zona reticularis secretes the steroid sex hormone adrenal androgen. The hormone is responsible for masculinising features. It also promotes bone growth and increases muscle mass.



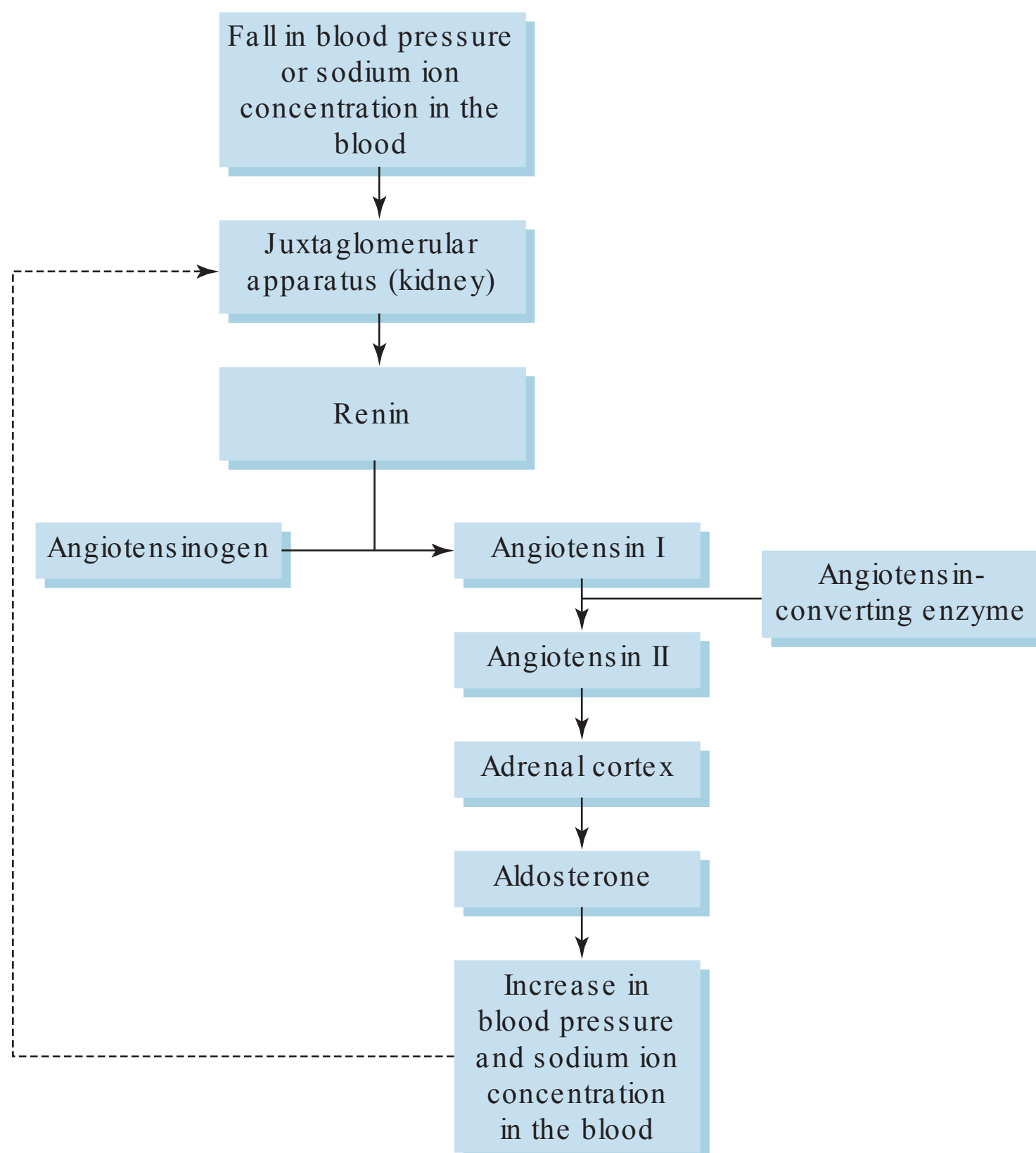
- (d) Catecholamines: Adrenal medulla secretes catecholamines. Catecholamines prepare the body for physical activity; they cause bronchial dilation, increased heart rate and cardiac output, and elevated blood glucose and lipolysis.

### Control of Adrenal Secretions

Hormones of adrenal cortex are under the control of negative feedback mechanism, whereas adrenal medulla secretion is under the control of sympathetic stimulation.

#### Aldosterone

- Secretion of aldosterone is under the control of negative feedback mechanism, which involves the renin–angiotensin system (Fig. 20.15).
- A fall in the blood pressure or sodium ion concentration in the blood causes the release of renin from juxtaglomerular cells of the kidney and this converts angiotensinogen into angiotensin I.
- Angiotensin I is converted into angiotensin II which stimulates the cells of zona glomerulosa to secrete aldosterone.
- As the blood pressure and sodium ion concentration rise and become normal, the release of renin is inhibited from the juxtamedullary apparatus.



**Figure 20.15** Negative feedback mechanism of aldosterone. Solid arrows indicate stimulatory effects and dashed arrow indicates inhibitory effects.

#### Glucocorticoids and Adrenal Androgens

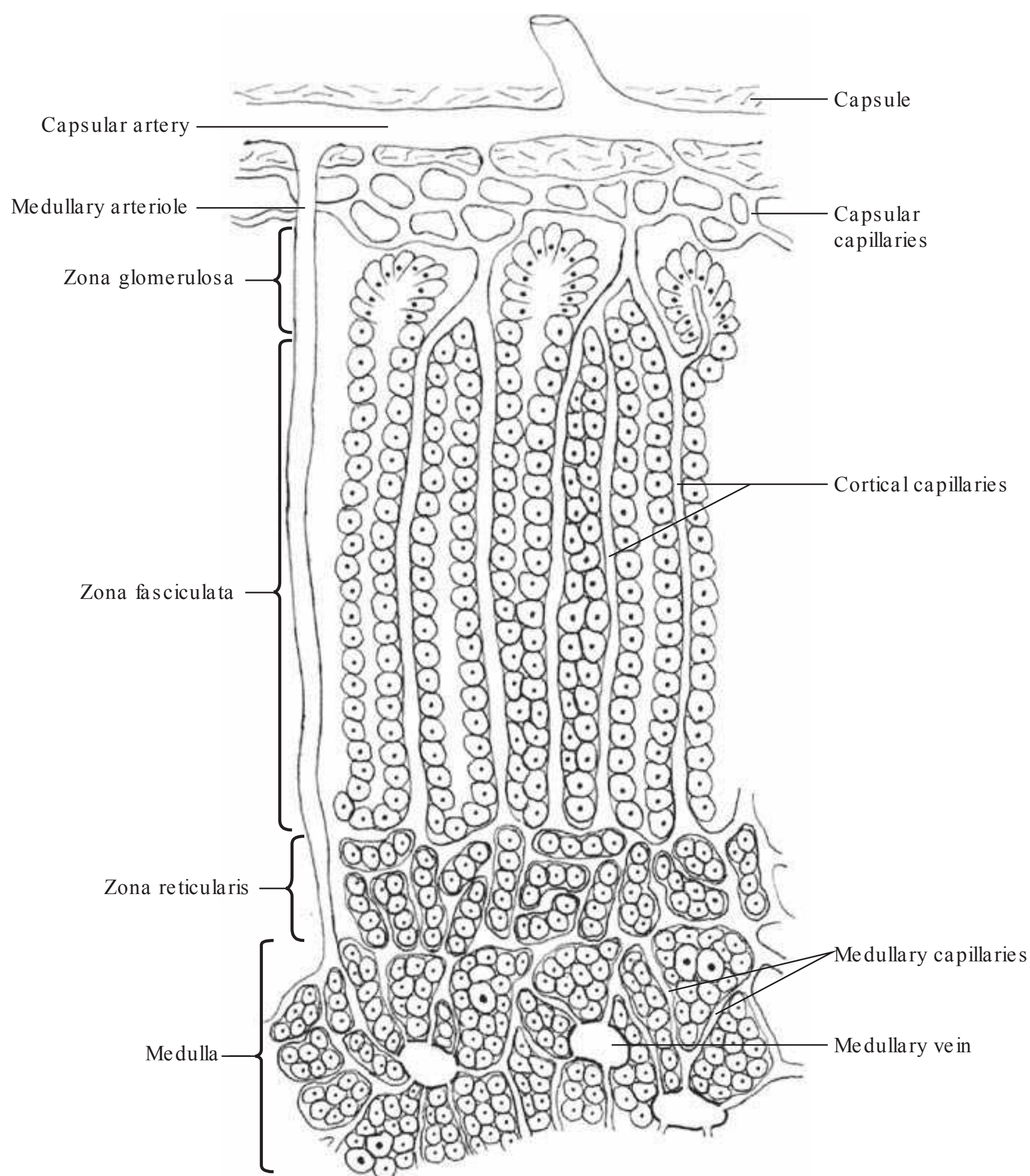
- Secretions of zona fasciculata and reticularis are under the control of ACTH, produced by adenohypophysis, through negative feedback mechanism (described under 'Control of Anterior Pituitary Secretion').

### *Catecholamines*

- As described earlier, the chromaffin cells of adrenal medulla are innervated by preganglionic sympathetic fibres, and they themselves correspond functionally to postganglionic sympathetic neurons.
- During sympathetic stimulation, chromaffin cells are stimulated by preganglionic sympathetic fibres and release the content of secretory granules by exocytosis.

### **BLOOD SUPPLY OF ADRENAL GLAND**

Superior, middle and inferior suprarenal arteries penetrate the capsule of the adrenal gland and supply the gland. Inside the gland, these arteries form three sets of capillaries: capsular, cortical and medullary (Fig. 20.16).



**Figure 20.16** Blood supply of the adrenal gland.



### Capsular Capillaries

- Small branches of superior, middle and inferior suprarenal arteries form a capillary plexus in the capsule.

### Cortical Capillaries

- Cortical capillaries begin from the blood vessels of the capsule.
- They pass through all three layers of cortex, between the cords of secretory cells.
- They drain into medullary capillaries.

### Medullary Capillaries

- Medullary capillaries are present in the medulla, surrounding the cords of secretory cells.
- They receive blood from two sources—from the cortical capillaries which empty into medullary capillaries and from medullary arterioles which begin from the arteries in the capsule, pass through the cortex without branching and enter the medulla. In the medulla, these arterioles branch to form medullary capillaries.
- Medullary capillaries drain into medullary veins (Fig. 20.16), and these small veins unite to form the suprarenal vein.

## CLINICAL CORRELATES

### Pituitary Adenoma

- It is the benign tumour of the pituitary and is the most common cause of hyperpituitarism. Pituitary adenomas are classified on the basis of hormone produced by the tumour cells. The most common pituitary adenoma is prolactinoma, which secretes prolactin and causes galactorrhoea, hypogonadism and infertility. It is treated by surgical excision.

### Thyroiditis

- Inflammation of thyroid is called thyroiditis. Hashimoto thyroiditis is an autoimmune disorder causing hypothyroidism, characterised by invasion of the thyroid parenchyma by leucocytes.

### Goitre

- Enlargement of the thyroid gland is called goitre. There are various causes for goitre—neoplastic, inflammatory, toxic (it has symptoms of hyperthyroidism) and simple goitre (gland is enlarged without any symptoms of hyperthyroidism or hypothyroidism).

### Hyperparathyroidism

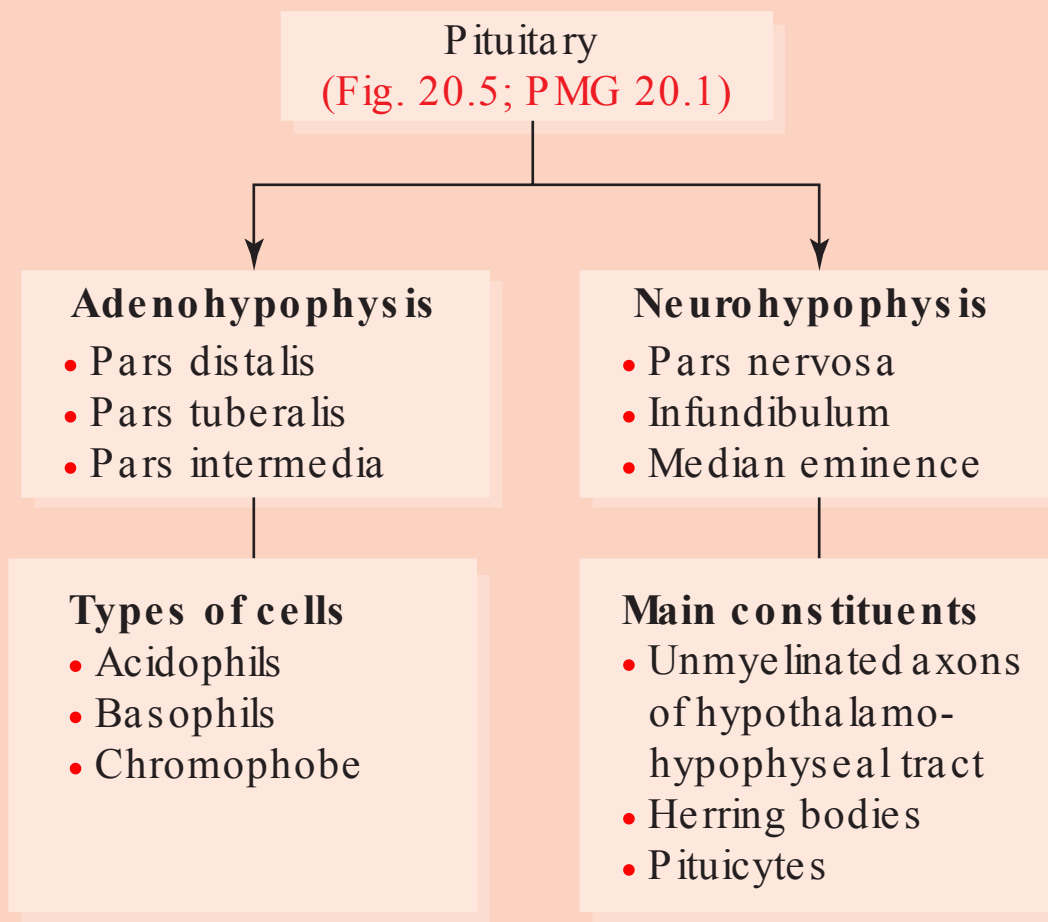
- Hyperparathyroidism is commonly due to adenoma, a benign tumour of parathyroid gland. Hypoparathyroidism is less common than hyperparathyroidism, usually seen after thyroidectomy, as parathyroid also gets excised along with the thyroid gland during the surgery.

### Hyperadrenalism

- Hyperplasia of adrenal cortex, the hormone-secreting tumour of the adrenal gland or the pituitary causes hyperadrenalism. Excess glucocorticoids level causes Cushing's syndrome and excess mineralocorticoid causes Conn's syndrome. Hypoadrenalism is caused by damage to the adrenal glands (autoimmune disease, congenital adrenal hypoplasia, tuberculosis, etc.), and it results in Addison's syndrome. Pheochromocytoma is the tumour of the chromaffin cells which produce and secrete catecholamines. Hypertension is the most common symptom.

# KEYPOINTS

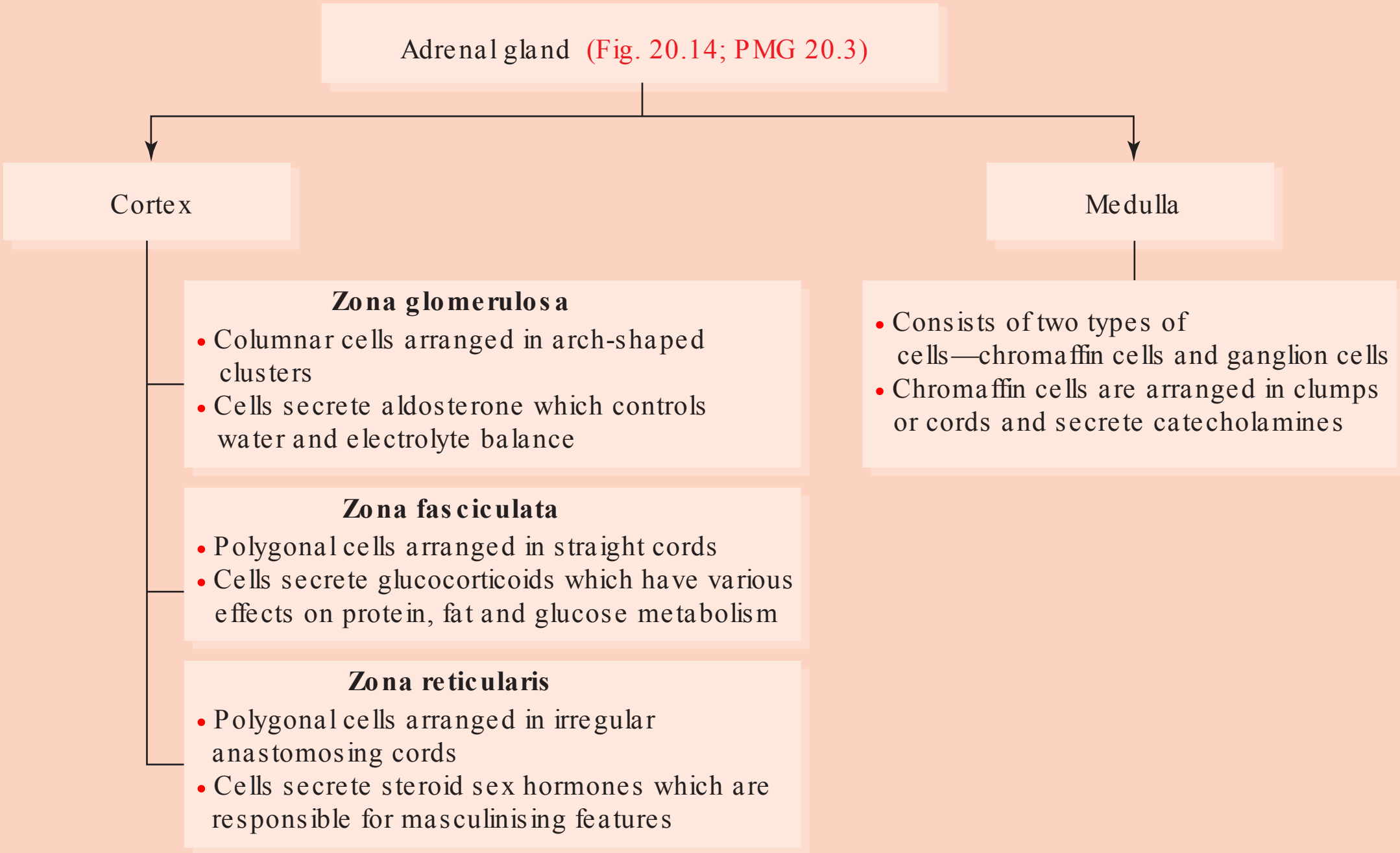
## Pituitary



## Thyroid and Parathyroid (Fig. 20.8; PMG 20.2)

Organ	Cell types and their organisation
Thyroid	Follicular cells—arranged in follicles
	Parafollicular cells—present in clusters in between the follicles; also present as single cells within the follicle
Parathyroid	Principal or chief cells—arranged in clumps or irregular cords
	Oxyphil cells—arranged in clumps

## Adrenal Gland





**SELF-ASSESSMENT**

1. What is the origin of the endocrine cells? How are these cells arranged?
2. Name the three major parts of the anterior pituitary.
3. What are the types of cells present in the anterior pituitary? How are they classified?
4. List the major components of the posterior pituitary.
5. Describe the microscopic structure and function of a thyroid follicle.
6. Where are the parafollicular cells located in the thyroid gland? Briefly discuss their function.
7. Name the types of cells present in the parathyroid gland. How are they arranged?
8. Which are the three layers of the adrenal cortex? Describe the arrangement of the cells in each layer and mention their secretions.
9. What are the types of cells present in the adrenal medulla?

# Central Nervous System

- The components of nervous tissue and the peripheral nervous system have been described in Chapter 8. This chapter describes the histology of the central nervous system.
- The central nervous system (CNS) consists of brain and spinal cord. The brain consists of (a) the cerebrum, which includes cerebral hemispheres and diencephalon, (b) the brain stem, which consists of medulla, pons and midbrain, and (c) the cerebellum.
- The entire CNS is surrounded by three membranes of connective tissue collectively known as the meninges (from outside to inside)—dura mater, arachnoid mater and pia mater.
- Histologically, like peripheral nervous system, the CNS also consists of neurons and glial cells. On gross appearance, most of the CNS is composed of white matter and grey matter (posterior pituitary and pineal glands are part of CNS, but they lack white and grey matter; refer Chapter 20). If a fresh specimen of brain or spinal cord is sliced, on the cut surface some parts appear white while some appear grey in colour; hence, they are known as white and grey matter respectively.
- White matter consists of axons of myelinated nerve fibres and glial cells. A few unmyelinated axons are also present. It does not contain cell bodies of the neurons.
- Grey matter contains cell bodies of the neurons, dendrites and unmyelinated parts of the axons and glial cells.

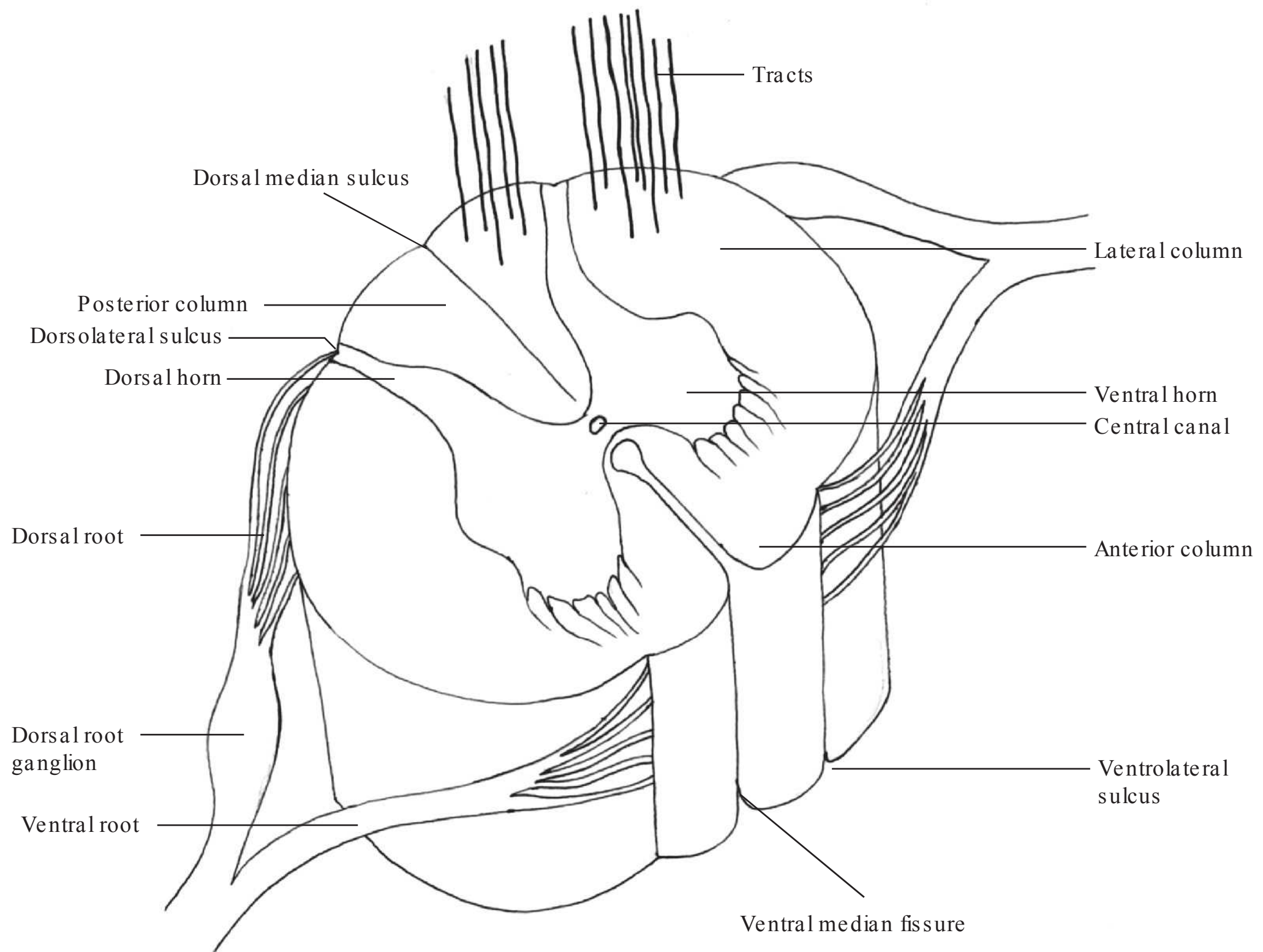
## SPINAL CORD

The spinal cord begins at the upper border of atlas vertebra, as a continuation of the medulla oblongata. It extends till the lower border of the first lumbar vertebra.

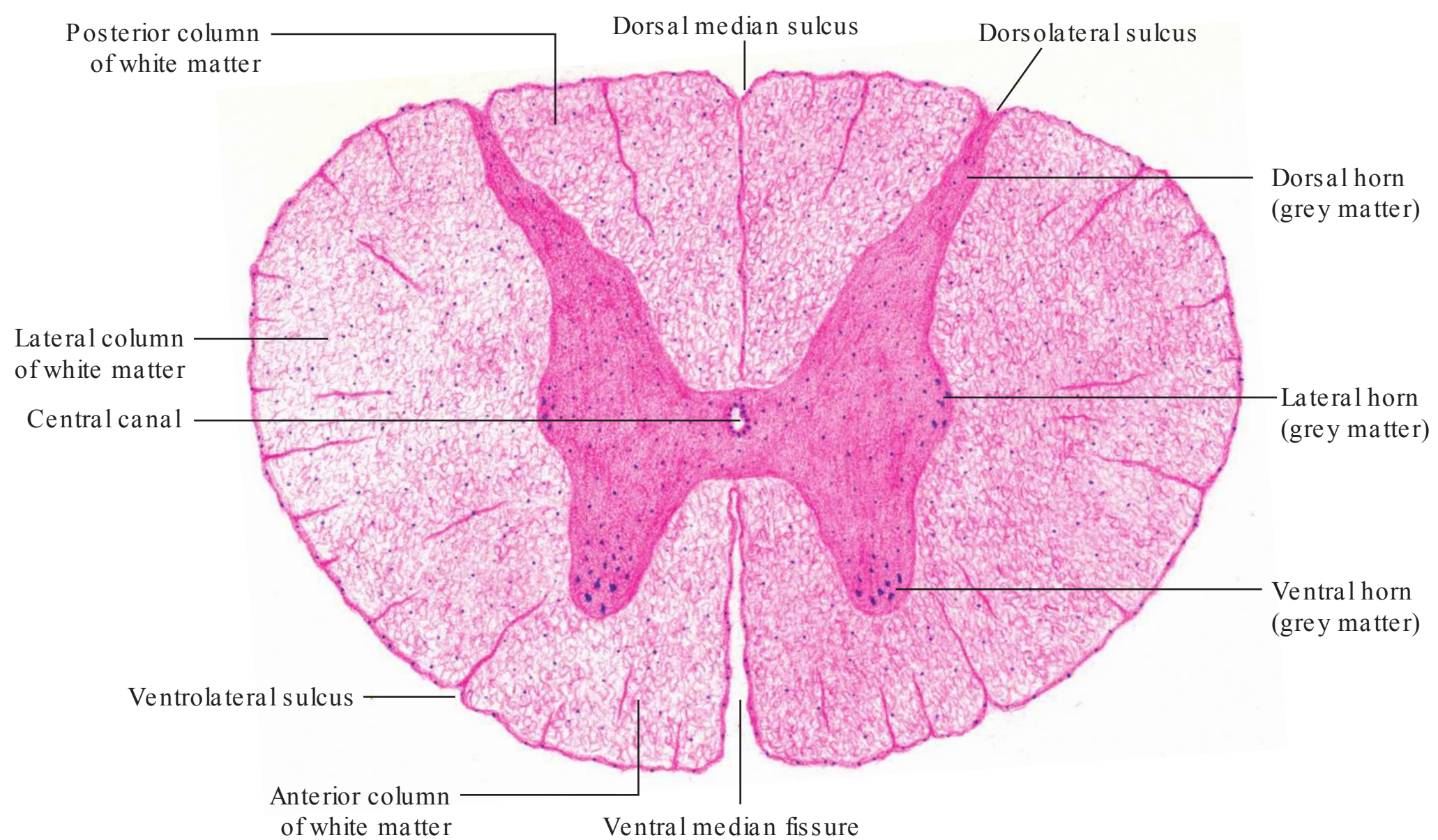
### STRUCTURAL ORGANISATION

- The spinal cord has a deep ventral median fissure with a ventrolateral sulcus on both its sides. There is also a shallow dorsal median sulcus with a dorsolateral sulcus on both its sides (Figs 21.1 and 21.2). The dorsal roots of spinal nerves enter the spinal cord at the dorsolateral sulcus, while the ventral roots emerge through the ventrolateral sulcus.
- A cross-section of the spinal cord shows H-shaped grey matter in the centre, which is surrounded by white matter (Figs 21.1 and 21.2).





**Figure 21.1** Transverse section of spinal cord (oblique view).



**Figure 21.2** Transverse section of spinal cord (thoracic segment) in low magnification (H&E pencil drawing).



### Grey Matter (Figs 21.1 and 21.2)

- The H-shaped grey matter consists of a pair of ventral and dorsal horns (or columns) and a central part which connects these horns. In thoracic segments of the spinal cord, a pair of lateral horns is also present.
- In the central part of the grey matter, there is a central canal lined by a single layer of columnar cells known as ependymal cells (a few ependymal cells have cilia—described in Chapter 8). The central canal contains cerebrospinal fluid.
- Ventral horns of the grey matter are very prominent. They contain the cell bodies of the lower motor (multipolar) neurons (Fig. 8.9, page 105), and the axons of these neurons emerge from the ventrolateral sulcus and form the ventral roots of spinal nerves.
- Dorsal horns are thinner than ventral horns. They contain central fibres of the pseudounipolar cells of dorsal root ganglion (Fig. 8.9, page 105) and cell bodies of the second-order sensory neurons of pain and temperature pathway.
- Lateral horns are present only in thoracic segments. Cells of this region give rise to preganglionic fibres of the sympathetic nervous system.

### White Matter

- The white matter consists of axons of ascending and descending tracts. It is subdivided into 3 pairs of columns—anterior, lateral and posterior columns (Figs 21.1 and 21.2).
- The anterior column lies between the ventral median fissure and the ventrolateral sulcus.
- The lateral column lies between the ventrolateral and dorsolateral sulci.
- The posterior column lies between the dorsal median sulcus and the dorsolateral sulcus.

### Coverings of Spinal Cord

- Coverings of spinal cord (from outside to inside) are dura mater, arachnoid mater and pia mater (described later in the chapter).

## CEREBELLUM

- The cerebellum is a part of the hind brain, located in the infratentorial compartment of the posterior cranial fossa.
- It plays an important role in coordination of voluntary movements and maintenance of the equilibrium and muscle tone.

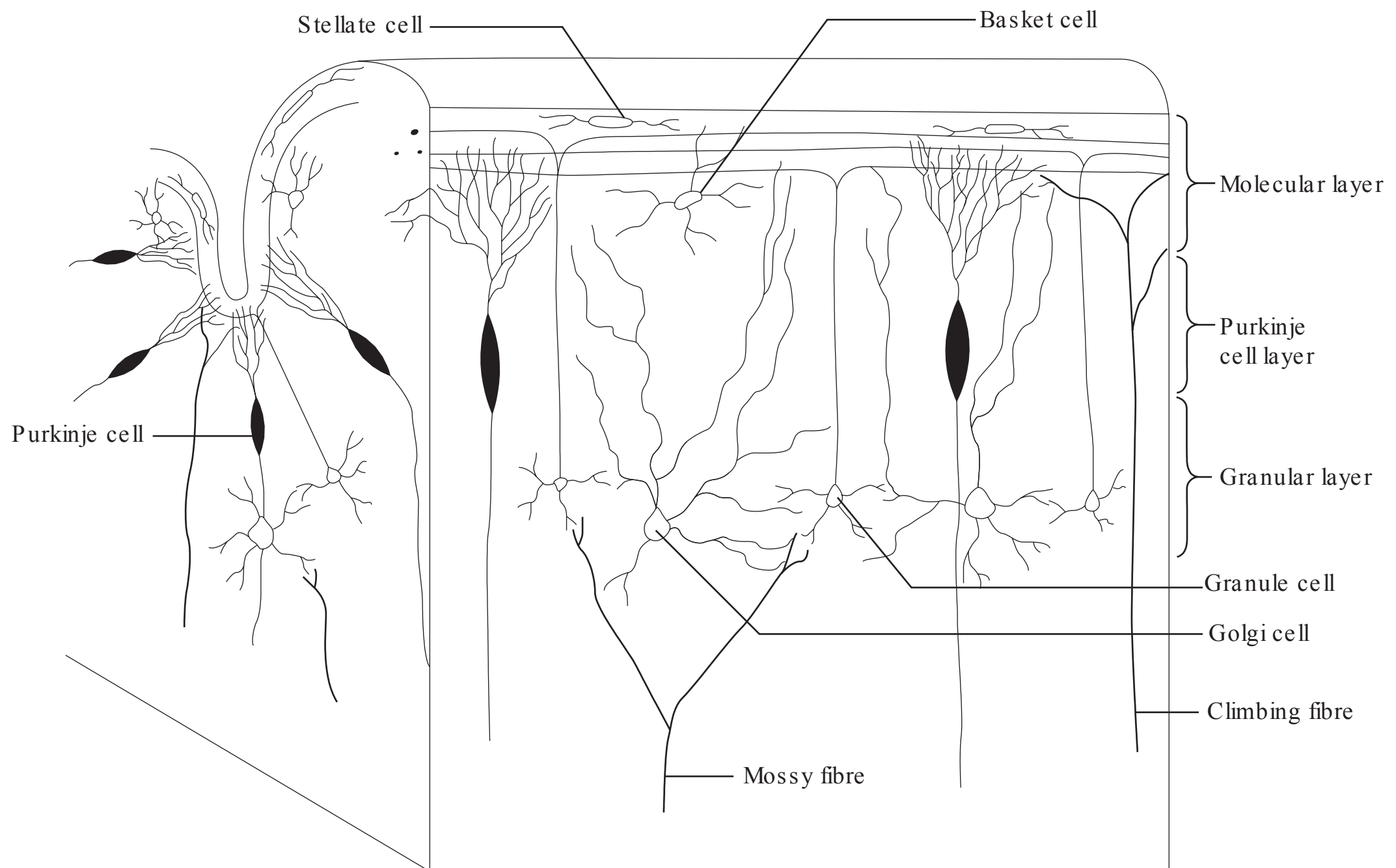
### NEURONS OF CEREBELLAR CORTEX

- The cerebellar cortex has the following five types of neurons: stellate, basket, Purkinje, Golgi and granule cells.
- Purkinje cells are large neurons with flask-shaped cell bodies. The other cells of the cerebellar cortex are small-sized neurons. Except granule cells, which are excitatory, the rest of the neurons are all inhibitory.
- Silver-stained histological slides of the cerebellar cortex reveal morphological details of these neurons.

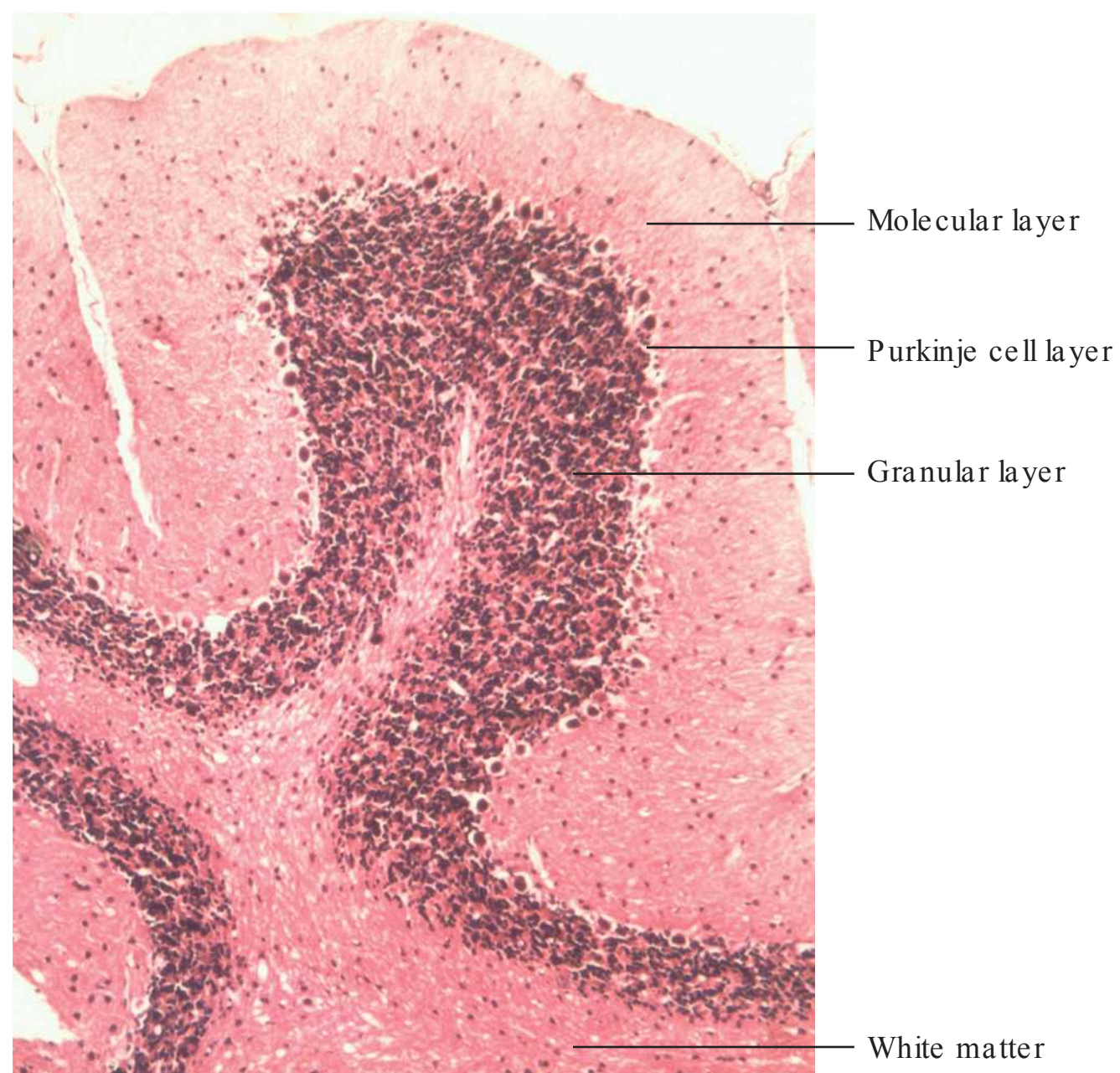


## STRUCTURAL ORGANISATION

Unlike the spinal cord, the cerebellum has a central core of white matter covered by grey matter. The cerebellar cortex shows numerous folds called folia (see Fig. 21.4a). The cerebellar cortex consists of three layers: the outer molecular, middle Purkinje and inner granular layers (Figs 21.3 and 21.4b; PMG 21.1).

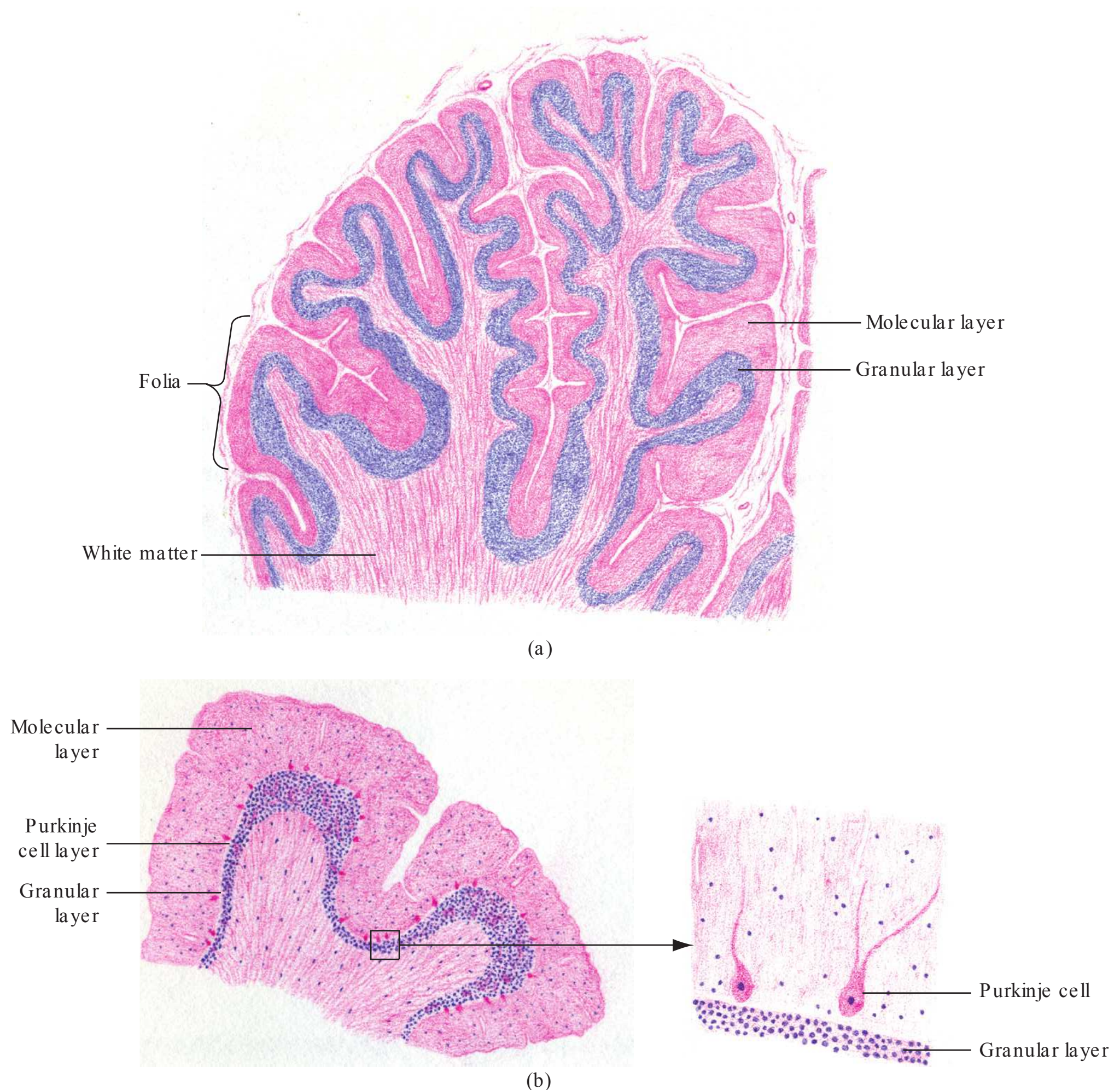


**Figure 21.3** Neurons of cerebellum and their organisation.



**PMG21.1** Cerebellum (H&Estain, X10).





**Figure 21.4** Section of cerebellum in (a) low magnification and (b) high magnification—inset shows a further magnified view of cerebellum (H&E pencil drawing).

### 1. Molecular layer (Fig. 21.3)

- This layer contains two types of neurons—stellate cells and basket cells. Stellate cells are in the outer zone and basket cells are in the inner zone.
- Dendrites of Purkinje cells and Golgi cells and axons of granular cells are also present in this layer.

### 2. Purkinje cell layer

- This layer contains a single layer of large, flask-shaped Purkinje cells (Figs 21.3 and 21.4b). These cells are oriented perpendicular to the surface of the folium.
- Dendrites of these cells extend into the molecular layer, where they synapse with climbing fibres (climbing fibres and mossy fibres are the two input fibres of the cerebellum).
- The axon of Purkinje cells arises from the base of the cell body and passes through the granular layer and enters the white matter.

### 3. Granular layer (Fig. 21.3)

- This layer is present between the Purkinje cell layer and the white matter of the cerebellum.
- This layer contains numerous small neurons—Golgi cells and granule cells.



- The axons of granule cells reach the molecular layer and bifurcate, and the branches of the axons run parallel to the folium and synapse with the dendrites of Purkinje cells.
- Dendrites of Golgi cells extend into the molecular layer and synapse with dendrites of granule cells and Purkinje cells and climbing fibres.
- These cells of the granular layer receive excitatory input from mossy fibres (input fibres).

## CEREBRUM

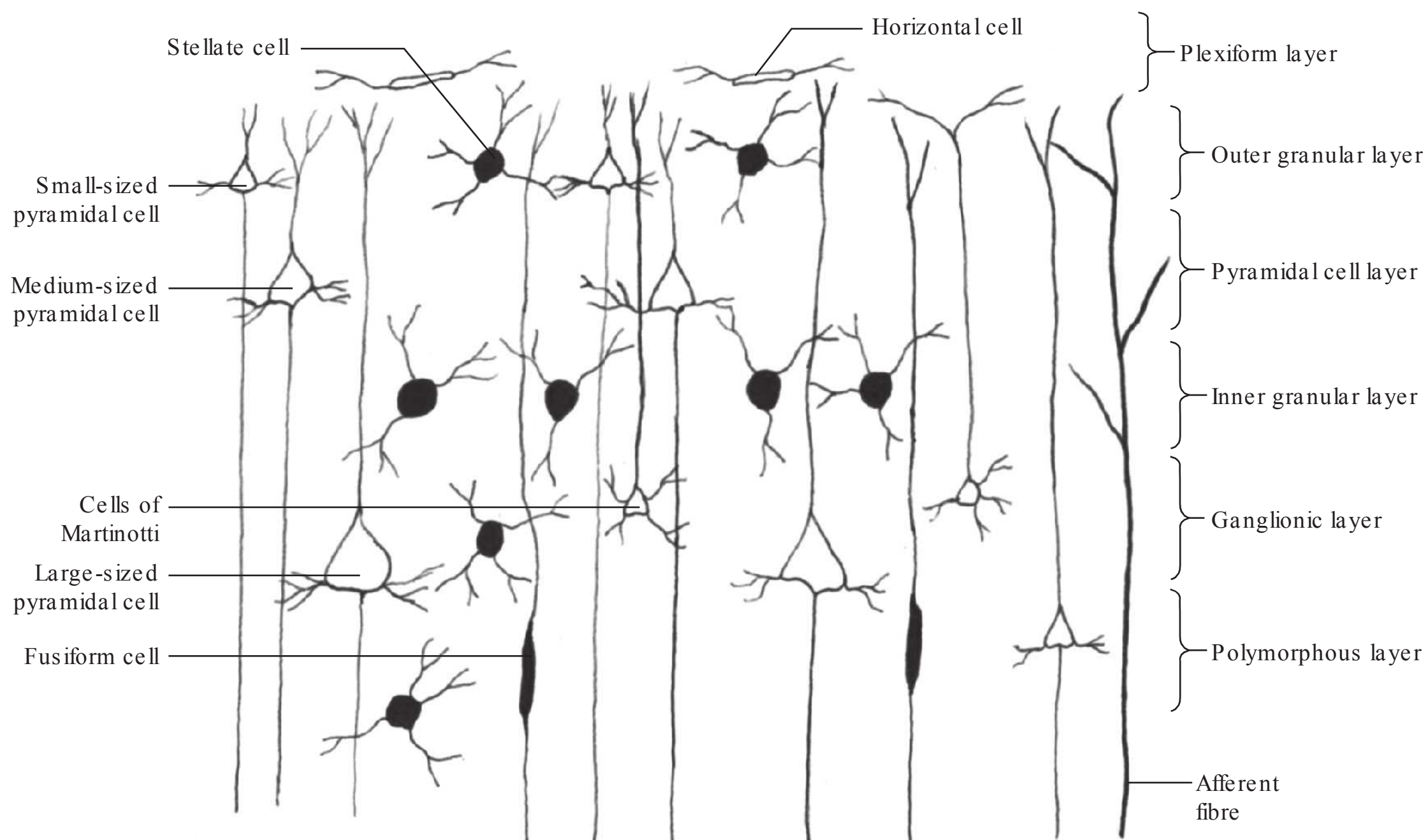
- Cerebrum is the largest part of the brain. The two cerebral hemispheres are separated by a median longitudinal fissure.
- The surface of the cerebrum has numerous folds separated by fissures—the folds are called gyri and the fissures are called sulci.
- Each gyrus has a central core of white matter, which is covered by a thin layer of grey matter. This thin layer of grey matter is the cerebral cortex.

### NEURONS OF THE CEREBRAL CORTEX (Fig. 21.5)

The cerebral cortex has the following five types of neurons: pyramidal cells, stellate cells, cells of Martinotti, horizontal cells of Cajal and fusiform cells. Morphological details of these neurons can be studied in silver-stained histological slides of the cerebral cortex.

#### 1. Pyramidal cells

- Cell bodies of these cells are pyramidal in shape and their apices are directed towards the surface of the brain.



**Figure 21.5** Neurons of cerebrum and their organisation.

- A long dendrite arises from the apex of the cell body, which extends into the superficial layers of the cerebral cortex. A few short dendrites arise from the base of the cell body and extend horizontally.
- The axon begins from the base of the cell body and enters the white matter of the cerebrum.
- These cells are classified on the basis of their size as small, medium and large.

## 2. Stellate cells

- These cells are also called granule cells.
- These cells have small, polygonal cell bodies.
- They have small dendrites which synapse with afferent fibres and neighbouring neurons.

## 3. Cells of Martinotti

- These are small cells with numerous small dendrites. Their axons extend into the superficial layer of the cortex.

## 4. Horizontal cells of Cajal

- These cells are fusiform in shape; their axons run parallel to the surface of the cortex.

## 5. Fusiform cells

- These cells are fusiform in shape, and they are oriented in the plane perpendicular to the surface of the cortex.
- Their axons and dendrites arise from the opposite poles of the cell body.

## STRUCTURAL ORGANISATION

The cerebral cortex consists of six layers, and there are no sharp boundaries between these layers. Six layers from superficial (towards the surface of the brain) to deep are as follows (Figs 21.5 and 21.6; PMG 21.2):

### 1. Plexiform or molecular layer

- This layer consists of horizontally oriented fibres which are derived from the processes of pyramidal, stellate and fusiform cells and cells of Martinotti. A few horizontal cells of Cajal are also present in this layer.

### 2. Outer granular layer

- This layer has numerous small pyramidal cells and stellate cells.

### 3. Pyramidal cell layer

- This layer has pyramidal cells of medium size.

### 4. Inner granular layer

- This layer consists of closely packed stellate cells.
- Densely packed horizontally running nerve fibres are collectively known as the outer band of Baillarger.

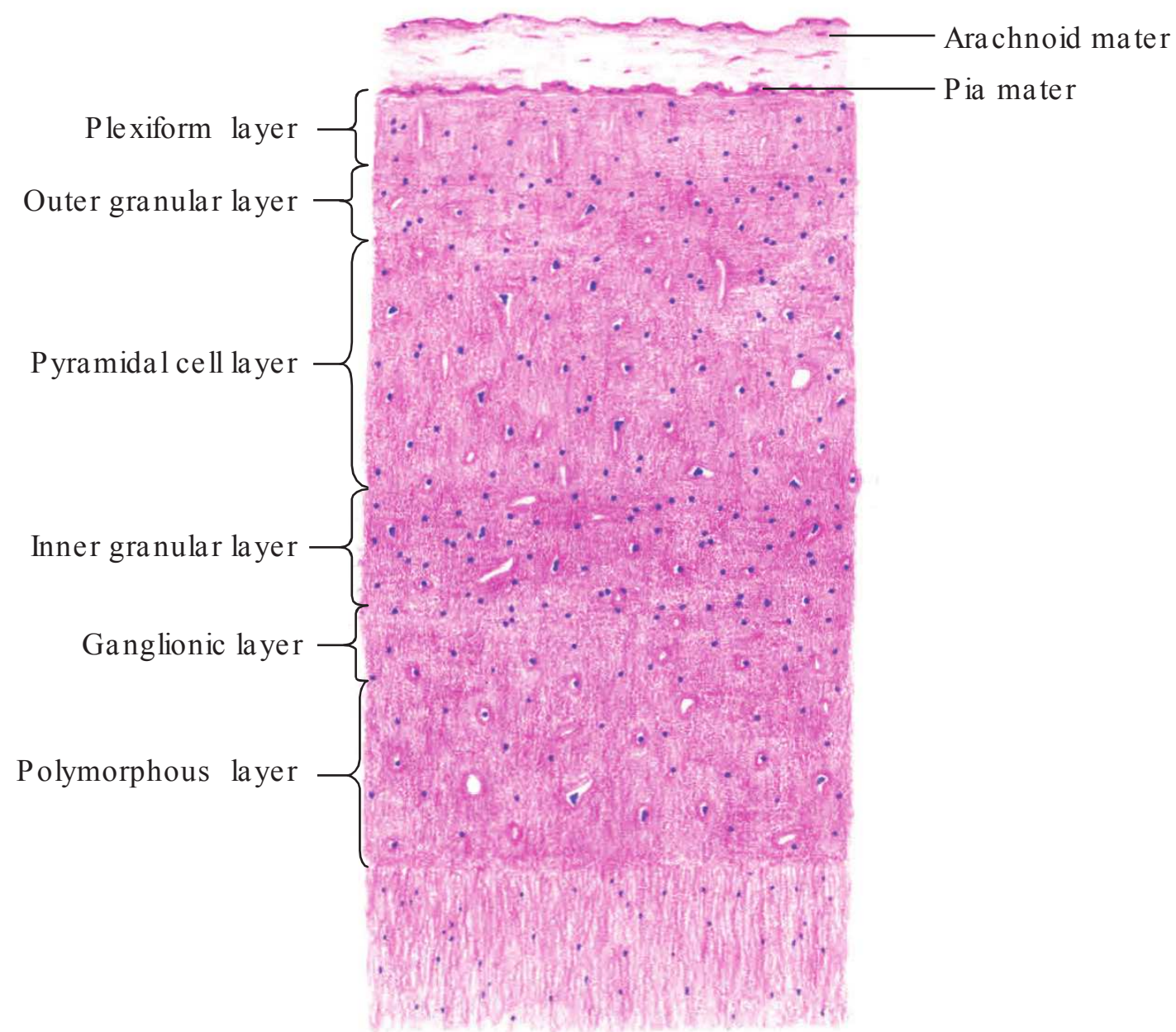
### 5. Ganglionic layer

- This layer has large pyramidal cells and a few granule cells and cells of Martinotti. Pyramidal cells of this layer are very large in the motor area, and they are called Betz cells.
- Densely packed horizontally running nerve fibres in this layer are collectively known as the inner band of Baillarger.

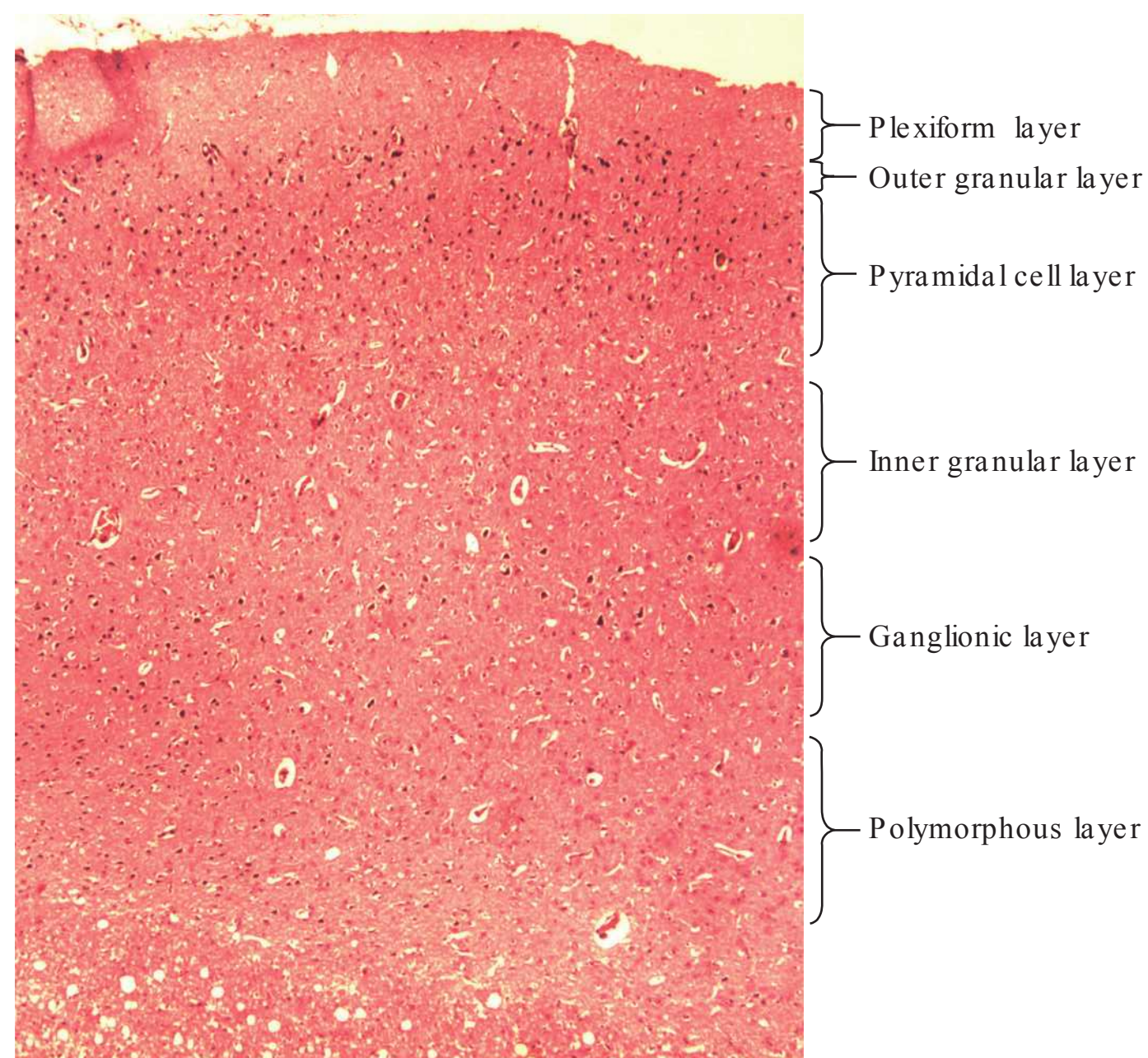
### 6. Polymorphous or multiform cell layer

- This layer contains cells of different shapes. It has small pyramidal cells, cells of Martinotti, a few stellate cells and fusiform cells.
- Fusiform cells are fusiform in shape and are oriented vertical to the surface.





**Figure 21.6** Section of cerebral cortex in low magnification (H&E pencil drawing).



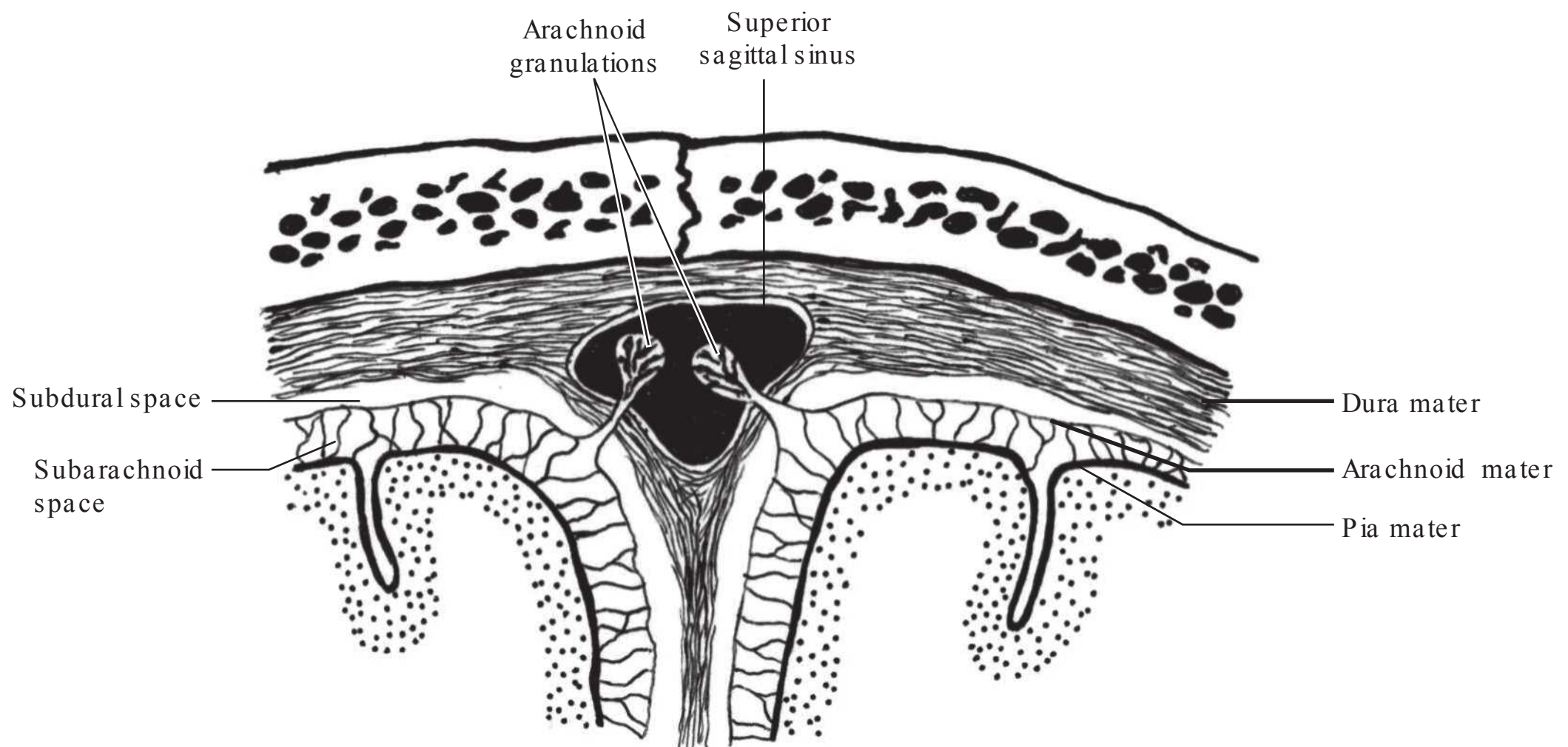
**PMG21.2** Cerebrum (H&E stain, X5).

## MENINGES

- Meninges are three layers of connective tissue surrounding the CNS. From superficial to deep, they are the dura mater, arachnoid mater and pia mater. Arachnoid mater and pia mater are collectively called leptomeninges (Fig. 21.6).



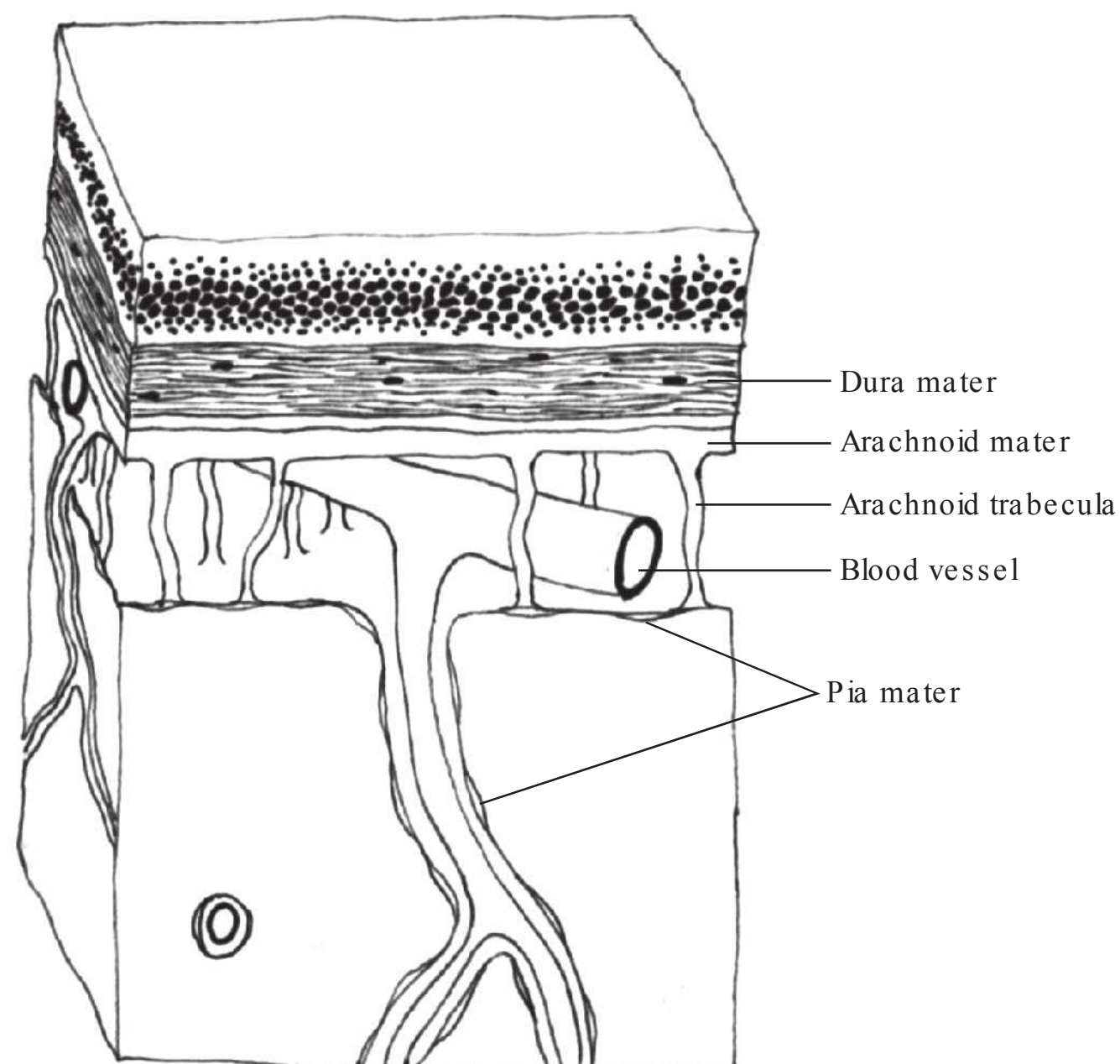
- Between the dura mater and the arachnoid mater, there is a subdural space (Fig. 21.7) containing a small volume of serous fluid.
- Between the arachnoid mater and the pia mater, there is a cerebrospinal fluid-containing space, the subarachnoid space (Fig. 21.7).



**Figure 21.7** Arachnoid granulations.

### **DURA MATER**

- The dura mater is composed of dense connective tissue (Figs 21.7 and 21.8).
- This is the outermost layer. In the brain, it further consists of two layers—outer endosteal and inner meningeal. The endosteal layer serves as the periosteum of the skull bones. As it continues



**Figure 21.8** Cerebral meninges (schematic diagram).



downwards, this layer gets attached to the margin of foramen magnum and thus it does not form a covering around the spinal cord. The meningeal layer continues in the spinal cord.

- In the spinal cord, dura consists of the meningeal layer only. It is separated from the periosteum of the vertebral canal by epidural space.

### ARACHNOID MATER (Figs 21.7 and 21.8)

- The arachnoid mater is a layer of connective tissue consisting of bundles of collagen fibres and fibroblasts.
- Both surfaces of the arachnoid are lined by mesothelium.
- Fine filaments arising from arachnoid mater extend between the arachnoid mater and the pia mater across the subarachnoid space.
- Arachnoid villi are small projections of arachnoid mater into the venous sinuses of brain; they pass through the dura mater. These villi act as one-way valves, and the cerebrospinal fluid present in subarachnoid space drains into the venous sinuses through these villi. Aggregations of these villi are called arachnoid granulations.

### PIA MATER

- The pia mater is the innermost layer of the meninges and it covers the CNS, lining each sulcus and fissure (Figs 21.7 and 21.8).
- It is a thin layer of vascular connective tissue containing collagen and elastic fibres and fibroblasts. It is lined by mesothelium.

## CLINICAL CORRELATE

### **Motor Neuron Disease (Amyotrophic Lateral Sclerosis)**

- Amyotrophic lateral sclerosis is the degenerative disorder of motor neurons (both upper motor and lower motor neurons). There is degeneration of the ventral horns of the spinal cord, and the ventral roots become thin. In the brain, there is degeneration of the upper motor neuron of the corticospinal tract. The disease manifests as asymmetrical weakness of the limb.

## KEYPOINTS

### **Spinal Cord (Figs 21.1 and 21.2)**

	Grey matter	White matter
Location	<ul style="list-style-type: none"> <li>• In the central part, H shaped</li> </ul>	<ul style="list-style-type: none"> <li>• In the peripheral part, surrounding the grey matter</li> </ul>
Parts	<ul style="list-style-type: none"> <li>• Ventral and dorsal horns</li> <li>• In thoracic segments, lateral horns</li> <li>• A central part which connects these horns</li> </ul>	<ul style="list-style-type: none"> <li>• Anterior, lateral and posterior columns</li> </ul>

### **Cerebellum (Figs 21.3 and 21.4; PMG 21.1)**

Layers (from superficial to deep)	Cells
1. Molecular	Stellate and basket cells
2. Purkinje cell	Purkinje cells
3. Granular layer	Golgi and granule cells

Cerebrum (Figs 21.5 and 21.6; PMG 21.2)

Layers (from superficial to deep)	Cells
1. Plexiform or molecular	Horizontal cells of Cajal and processes of pyramidal, stellate and fusiform cells and cells of Martinotti
2. Outer granular	Pyramidal cells and stellate cells
3. Pyramidal cell	Medium-sized pyramidal cells
4. Inner granular	Stellate cells
5. Ganglionic cell	Granule cells and cells of Martinotti, Betz cells in motor cortex
6. Polymorphous cell	Small pyramidal cells, cells of Martinotti, a few stellate cells and fusiform cells

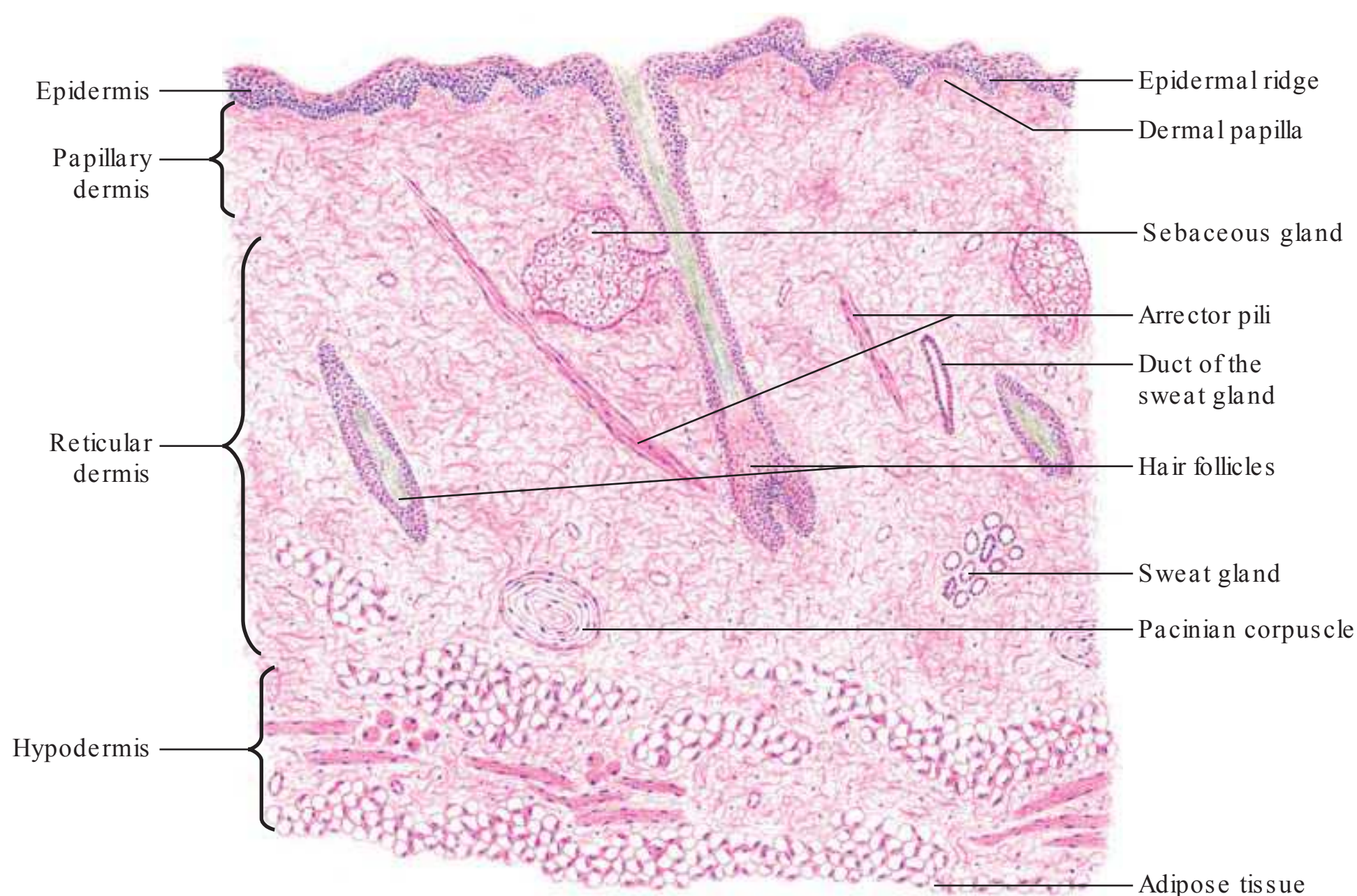
SELF-ASSESSMENT

1. Describe the internal features of the spinal cord.
2. What are the three layers of cerebellar cortex? List the types of cells present in each layer.
3. What are the layers of cerebral cortex? What are the types of cells present in each layer?



# Skin

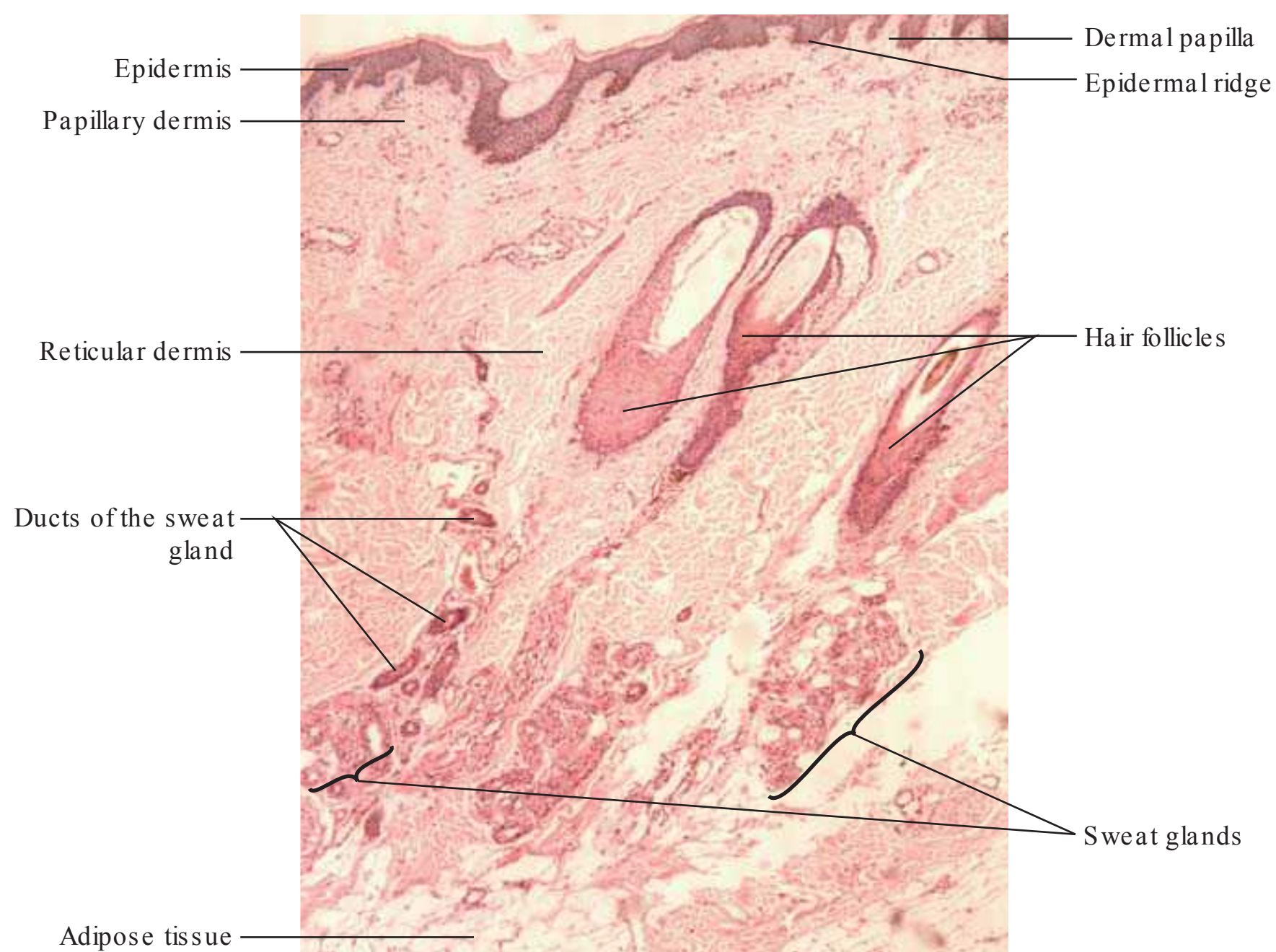
- Skin is the largest organ of the body and constitutes about 16% of the body weight. It covers the entire exterior of the body. Its thickness varies from 0.5 to 5 mm in different parts of the body.
- Skin consists of two layers: the outer layer epidermis and the underlying layer dermis (Fig. 22.1).
- Skin is classified as thin and thick based on the thickness of epidermis. The thickness of epidermis in thin skin is around 0.1 mm and in thick skin it is around 0.5 mm. Thick skin is present in the palm and sole, and the rest of the body is covered by thin skin.
- Beneath the skin (i.e. subcutaneously), there is a layer of loose connective tissue and adipose tissue, the hypodermis.



**Figure 22.1** Section of thin skin in low magnification (H&E pencil drawing).



- The epidermis is made up of an epithelium; it is of ectodermal origin and is innervated by free nerve endings. It is an avascular structure and gets its nourishment from the blood vessels in the dermis.
- The dermis consists of connective tissue; it develops from mesoderm.
- At the junction of epidermis and dermis, the dermis has upward projections called dermal papillae which interdigitate with downward projections of epidermis called epidermal ridges (Fig. 22.1; PMG 22.1). The skin over the dermal papillae produces ridges on the skin surface, and these ridges determine the pattern of fingerprints.
- Functions
  - (a) Protection
    - (i) Epidermis acts as a mechanical barrier, prevents the entry of foreign material and makes the external surface of the body water resistant.
  - (b) Sensation
    - (i) Skin has various sensory receptors for different types of sensations (pain, pressure, touch and temperature). Refer Chapter 23 for more details.
  - (c) Thermoregulation
    - (i) When the external temperature is high or during physical exercise, sweating is increased. Evaporation of sweat from the body surface reduces the body temperature.
    - (ii) When the external temperature is low, blood flow to the skin is reduced by vasoconstriction of the blood vessels in the dermis to prevent heat loss.
    - (iii) Adipose tissue in the hypodermis acts as an insulator.

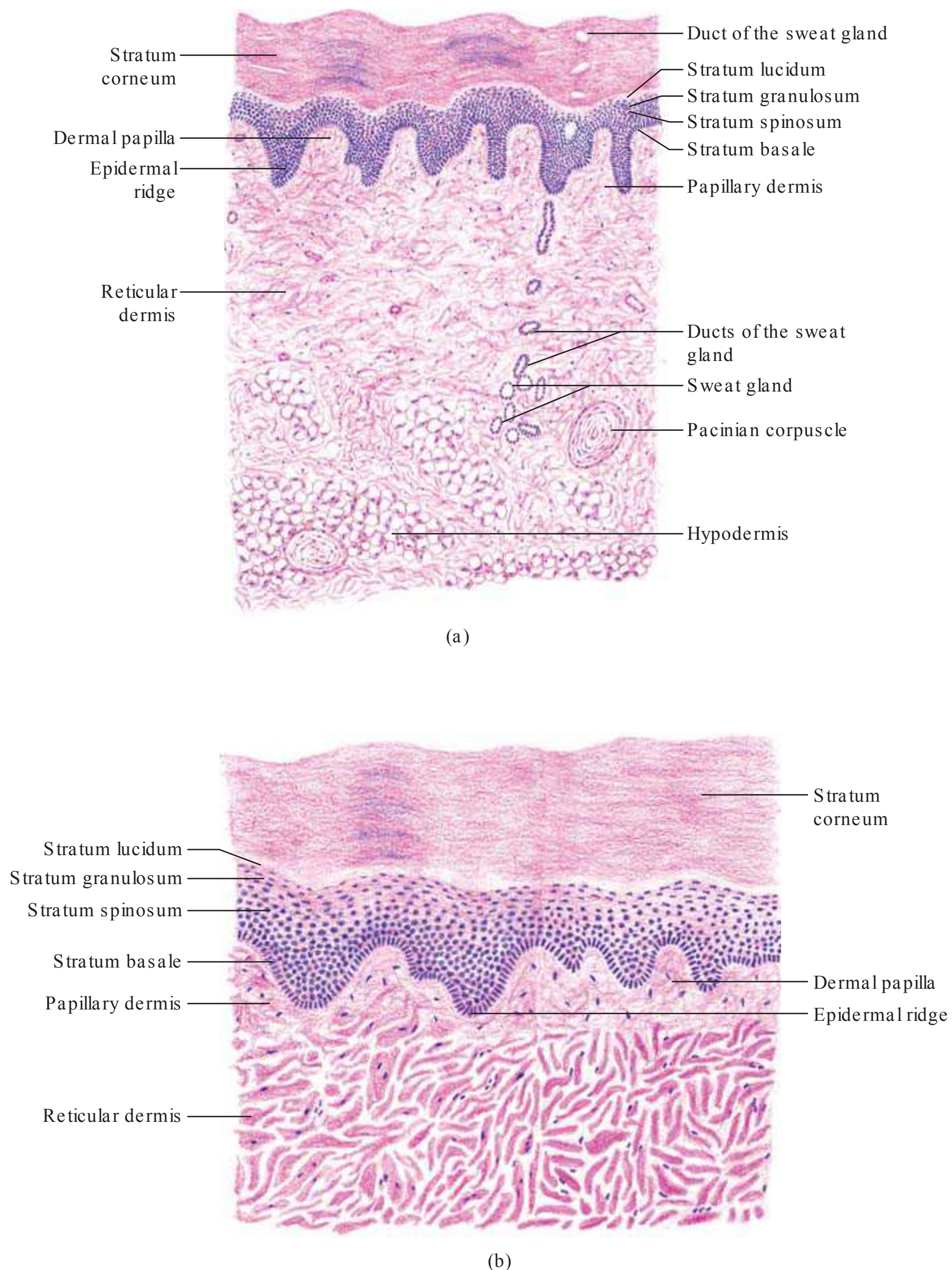


**PMG 22.1** Thin skin (H&E stain, X5).



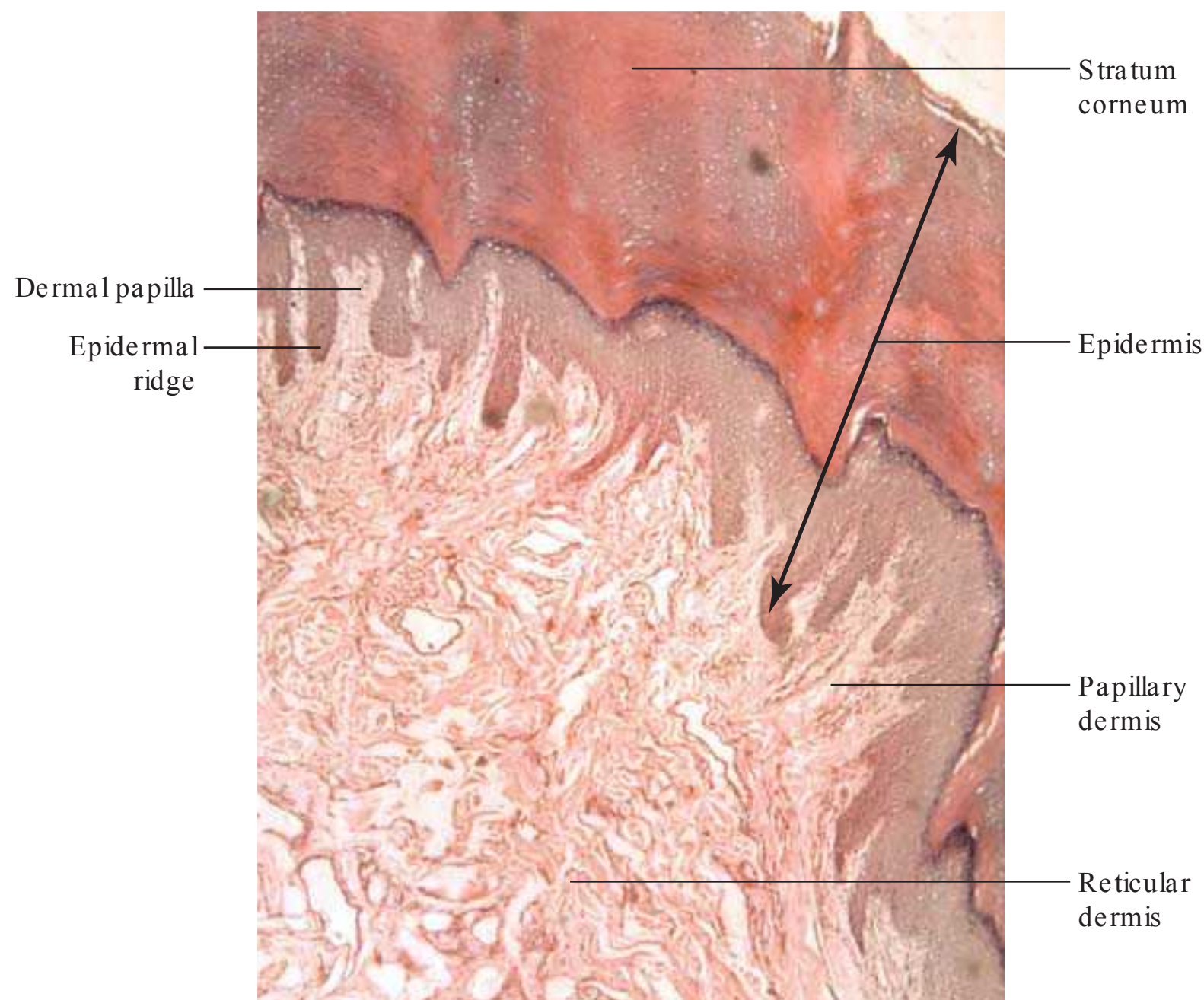
## EPIDERMIS

- The epidermis is made up of keratinised stratified squamous epithelium.
- It consists of two types of cells: keratinocytes and non-keratinocytes. Majority of the cells in epidermis are keratinocytes; non-keratinocytes include melanocytes, Langerhans cells and Merkel cells.
- It is composed of the following five layers (from deepest to most superficial): stratum basale or stratum germinativum, stratum spinosum, stratum granulosum, stratum lucidum and stratum corneum (Fig. 22.2; PMG 22.2).



**Figure 22.2** Section of thick skin in (a) low magnification and (b) high magnification (H&E pencil drawing).





**PMG 22.2** Thick skin (H&E stain, X5).

## LAYERS OF EPIDERMIS

Apart from the thickness of the epidermis, thin skin differs from thick skin in that stratum lucidum is absent in thin skin.

### 1. Stratum basale (or stratum germinativum)

- It is the deepest layer of the epidermis and hence it is closest to the dermis.
- It consists of a single layer of columnar or cuboidal-shaped keratinocytes, resting on the basement membrane.
- Cells of this layer divide and replenish the cells in more superficial layers.
- Cells are attached to the neighbouring cells by desmosomes and to the basement membrane by hemidesmosomes.

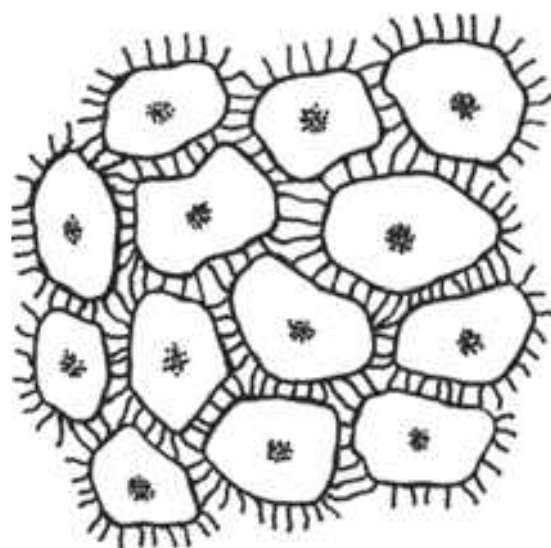
### 2. Stratum spinosum

- It consists of several layers of keratinocytes, overlying the stratum basale.
- In the deeper layers of stratum spinosum, cells are polygonal with spherical nuclei. Cells and their nuclei gradually flatten as they move towards the superficial layer.
- These cells have cytoplasmic projections which give spine-like appearance to them; hence these cells are also called prickly cells (Fig. 22.3).
- Desmosomes attach to the cytoplasmic projections of the neighbouring cells.
- Malpighian layer: Stratum basale and spinosum together are referred to as Malpighian layer. Mitotic activity in the epidermis is limited only to this layer.

### 3. Stratum granulosum

- It consists of four to five layers of flattened cells, the long axes of cells being parallel to the skin surface.
- Nuclei and cell organelles are present only till this layer; the cells in the layers superficial to stratum granulosum do not have nuclei and cell organelles.
- The cytoplasm of these cells contains numerous keratohyalin granules. Contents of these granules are released to fill the interstitial space, which is important for the functioning of the epidermis as a barrier.





**Figure 22.3** Prickle cells in stratum spinosum.

#### 4. Stratum lucidum

- It consists of several layers of flattened dead cells.
- It appears as a narrow translucent layer superficial to the stratum granulosum.
- Nuclei and other cell organelles are not seen, and cytoplasm has abundant keratin filaments.
- This layer is not apparent in thin skin.

#### 5. Stratum corneum

- It consists of 15–20 layers of dead keratinised cells.
- Cells are very flat; without cell organelles, the cytoplasm has abundant keratin filaments.
- Cells are constantly shed from the stratum corneum and are replaced by underlying cells.

### NON-KERATINOCYTES

As mentioned earlier, epidermis consists of two types of cells, that is keratinocytes and non-keratinocytes. Keratinocytes are the majority type. Three more types of cells which are seen in epidermis are melanocytes, Langerhans cells and Merkel cells.

#### 1. Melanocytes

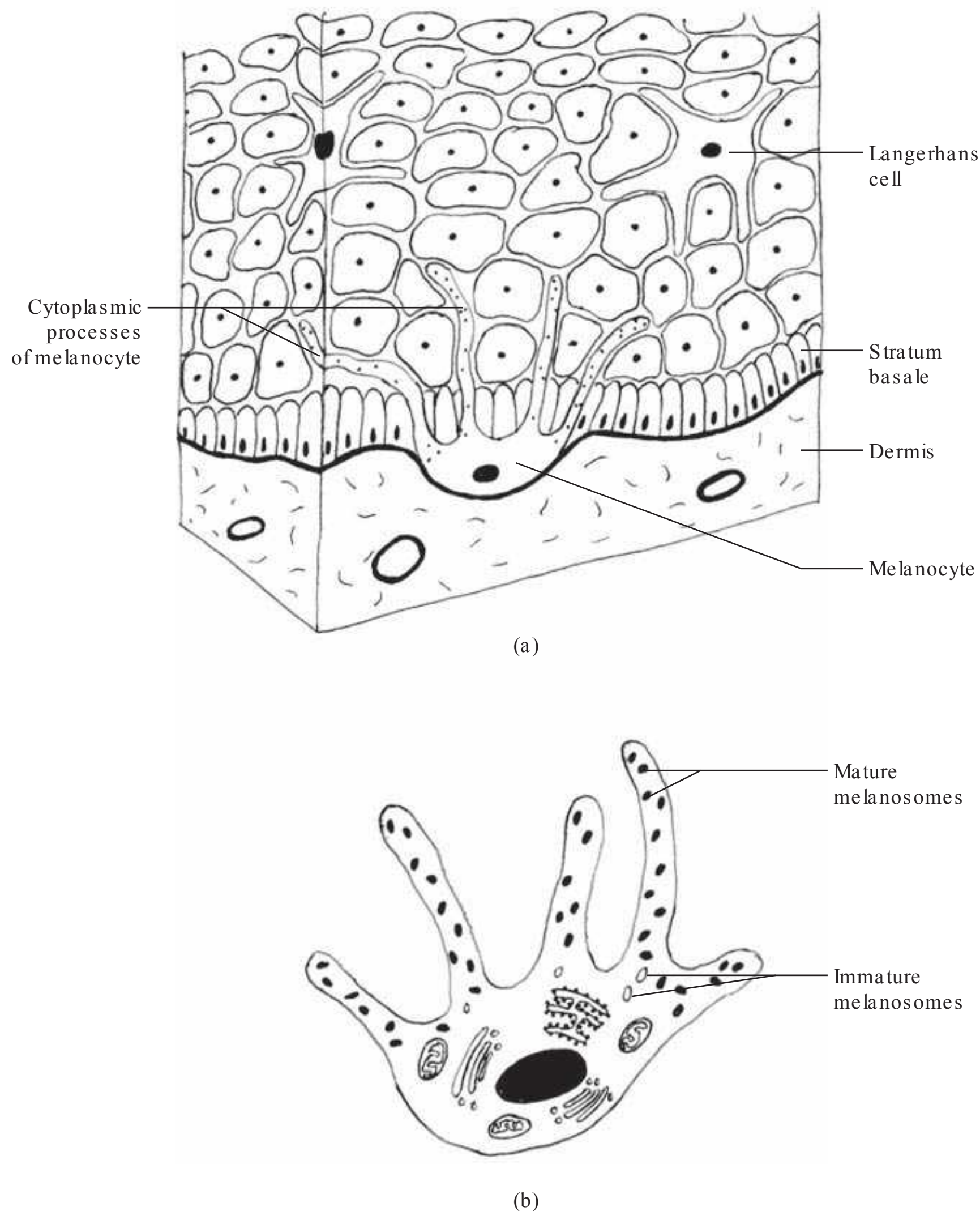
- Melanocytes originate from neural crest.
- They are located between basal cells and basement membrane of epidermis (Fig. 22.4). These cells are difficult to visualise in the H&E-stained histological slide.
- They have abundant cytoplasm with a large oval nucleus. These cells send cytoplasmic processes between the cells of stratum spinosum (Fig. 22.4).
- They produce the pigment melanin, which is responsible for skin colour and provides protection against ultraviolet radiation.
- Melanin synthesis occurs in membrane-bound organelles known as melanosomes present in the cytoplasm of the melanocytes. As more melanin is formed, melanosomes mature and migrate towards the tips of the cytoplasmic processes of the melanocytes. Mature melanosomes are present at the tips of the cytoplasmic processes of melanocytes, and from here they are transferred to neighbouring cells.

#### 2. Langerhans cells

- These cells are present in the stratum spinosum (Fig. 22.4). They are not seen in the H&E-stained histological slide.
- They are derived from bone marrow.
- They are similar to the dendritic cells of lymphoid tissue. Single they have a role in immune reactions (antigen-presenting cells) of the epidermis.

#### 3. Merkel cells

- Merkel cells are sensory mechanoreceptors located in stratum basale.
- They have desmosomal attachments with the adjacent cells. Also see 'Merkel's Corpuscles' described in Chapter 23.

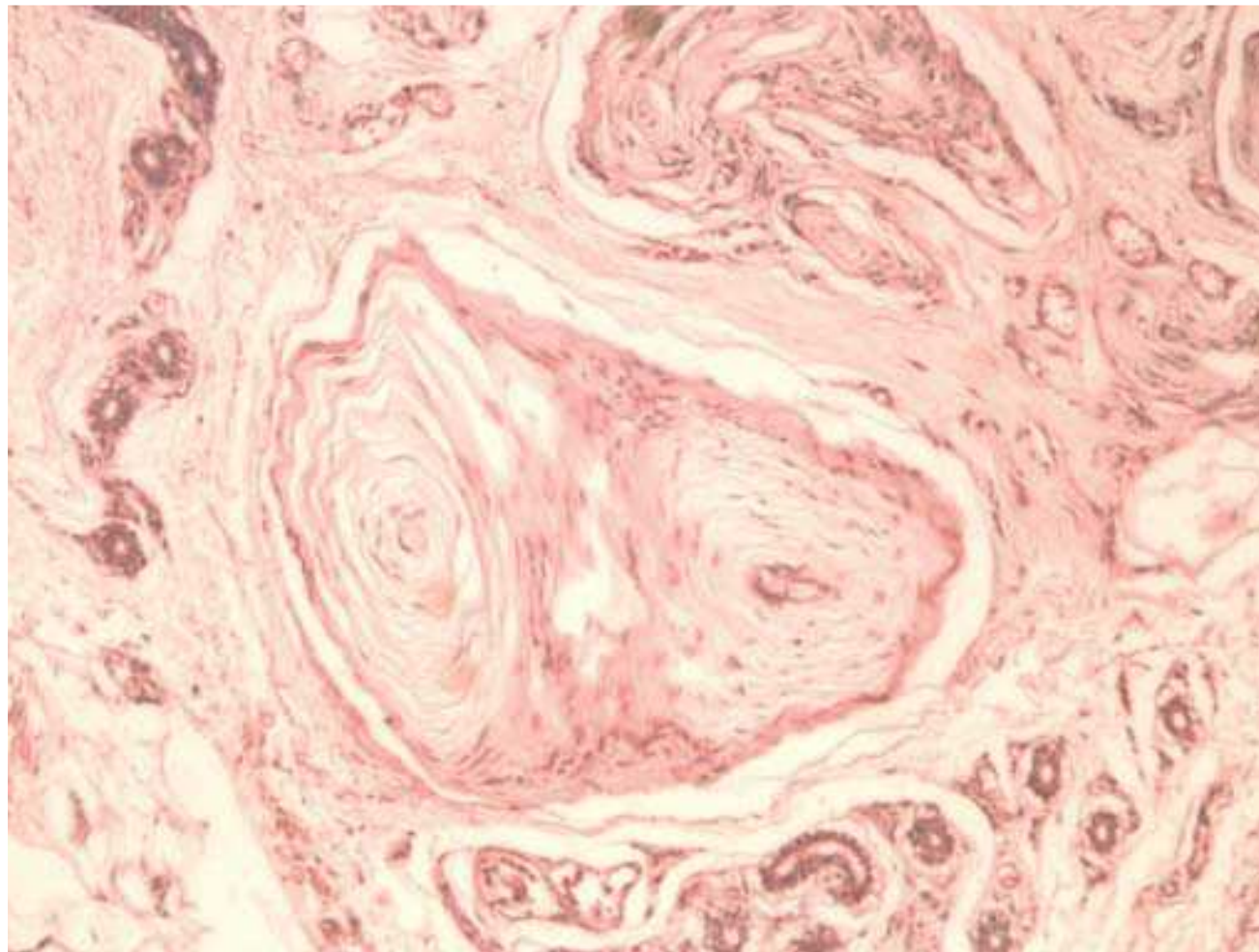


**Figure 22.4** Schematic diagram of skin showing (a) melanocytes and Langerhans cells in the layers of epidermis and (b) detailed structure of a melanocyte.

## DERMIS

- Dermis consists of two layers: papillary and reticular dermis (Figs 22.1 and 22.2; PMG 22.1 and 22.2).
- Papillary dermis is superficial and consists of loose connective tissue.
- Reticular dermis is deep and consists of irregular dense connective tissue.
- Papillary dermis forms dermal papillae at the junction of epidermis, which interdigitate with downward projections of epidermis called epidermal ridges. The skin, which is subjected to more mechanical stress (skin of palm and sole), has long epidermal ridges and dermal papillae.
- Dermis is vascular, and it has rich supply of free nerve endings and Pacinian corpuscles (Figs 22.1 and 22.2a; PMG 22.3). Pacinian corpuscles are cutaneous receptors (they are described in Chapter 23, under the section 'Cutaneous Receptors').





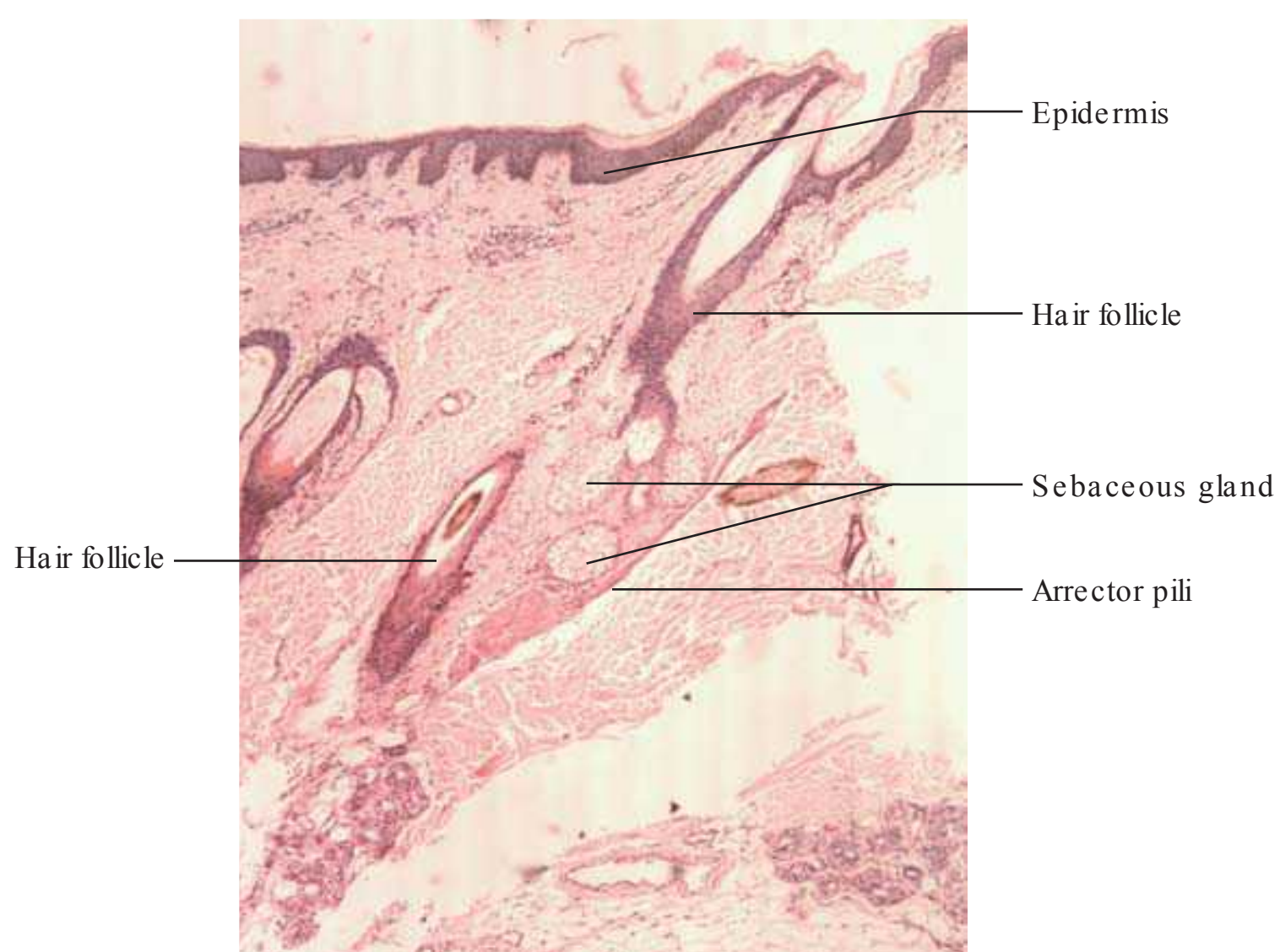
**PMG 22.3** Pacinian corpuscle (H&Estain, X5).

## SKIN APPENDAGES

Hair follicles, nails and sweat and sebaceous glands are derived from epidermis and collectively called the appendages of the skin.

### HAIR FOLLICLE

- It is present in thin skin (Fig. 22.1; PMG 22.4).
- It is derived from tubular invagination of the epidermis into the dermis.
- The lower end of the hair follicle is embedded in dermis, and it forms an enlargement, the bulb, which consists of actively dividing cells.



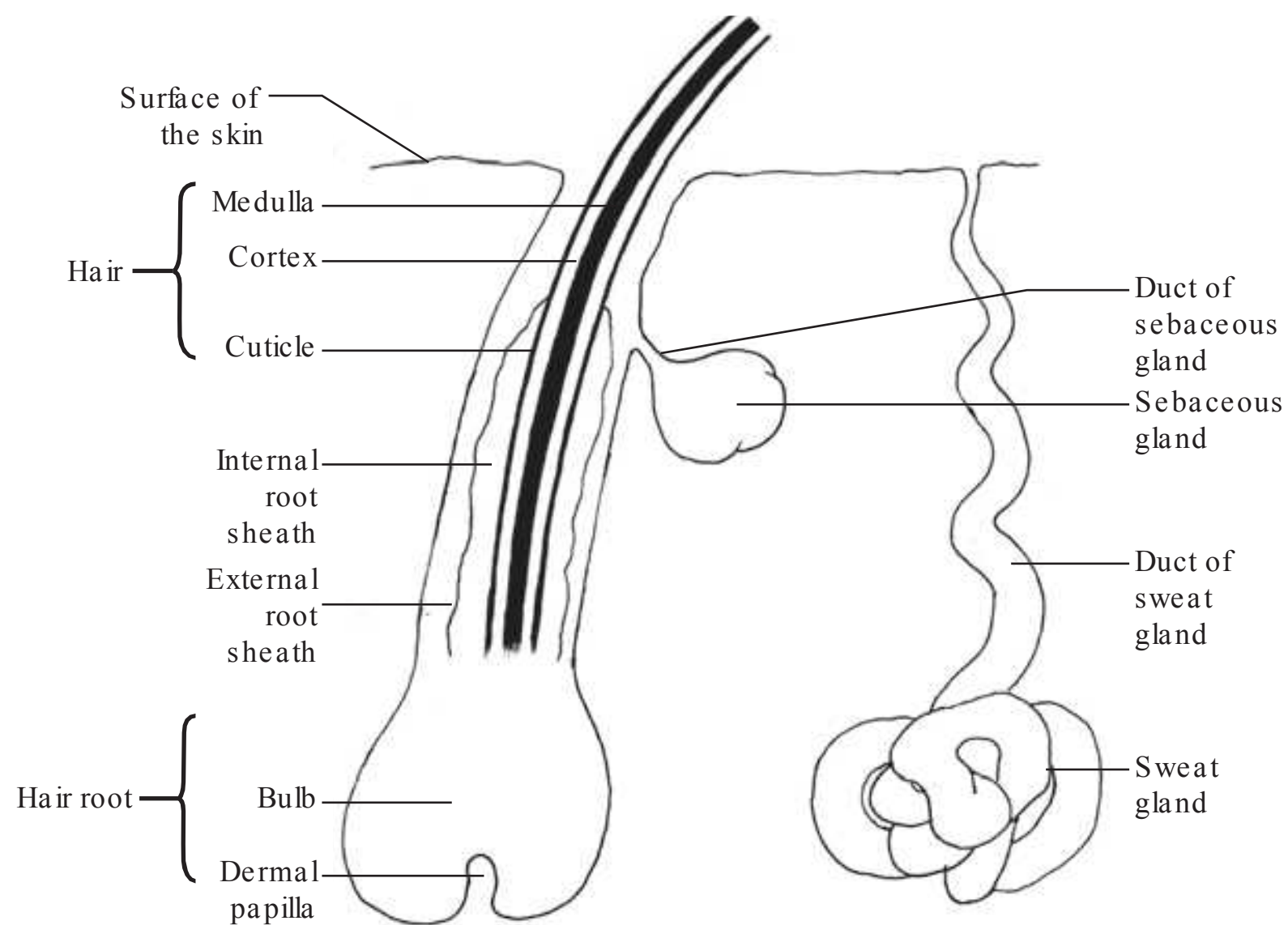
**PMG 22.4** Section of thin skin showing the pilosebaceous apparatus, which includes hair follicle, associated sebaceous glands and arrector pili muscle (H&Estain, X5).



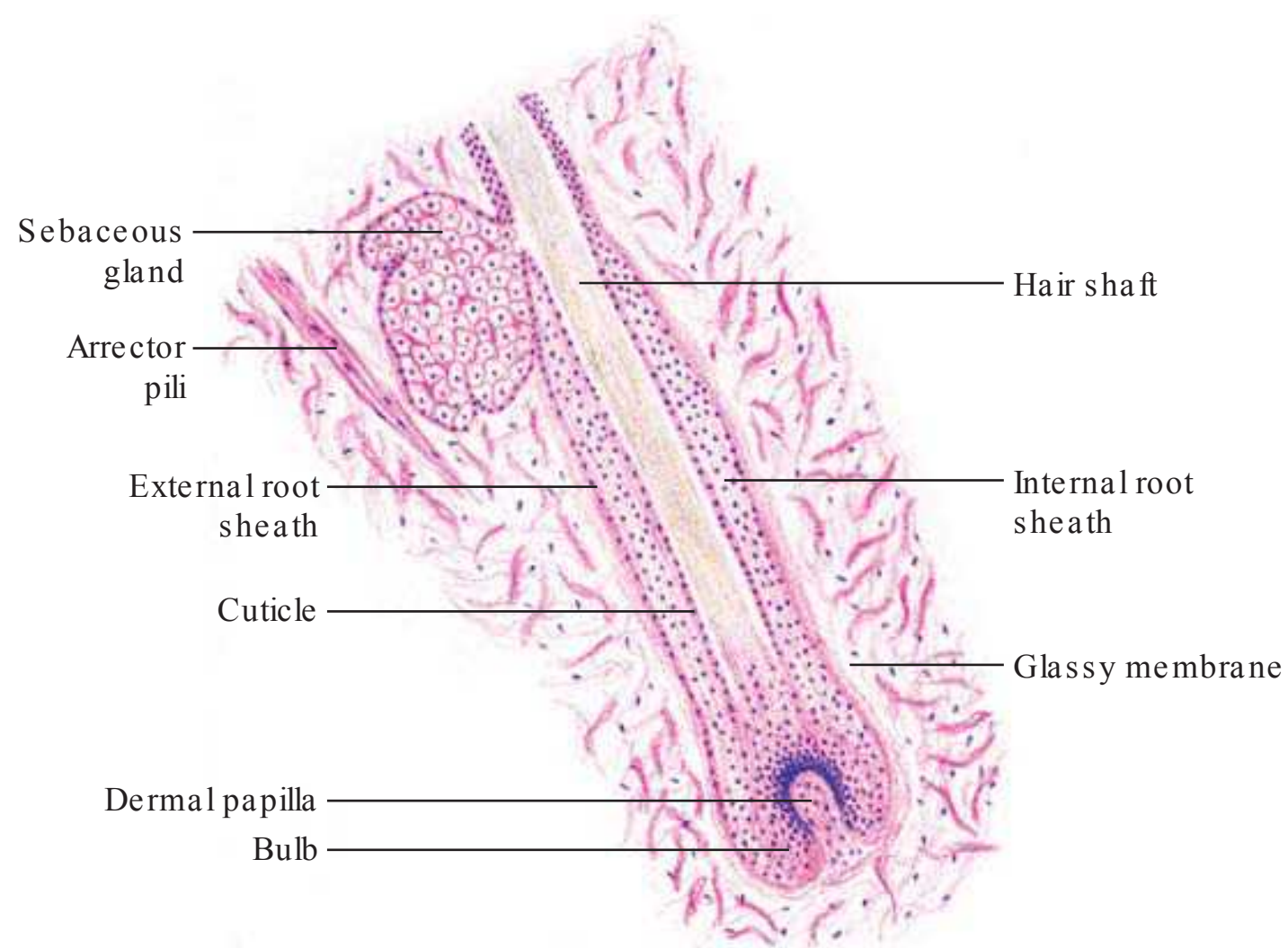
- The bulb encloses a connective tissue papilla called the dermal papilla. The entire mass of the bulb along with enclosed dermal papilla is called hair root (see Figs 22.5 and 22.6). Dermal papilla contains a capillary plexus and nerve endings.
- Cells in the bulb divide and their progeny differentiates into the cell types which form the hair shaft or the hair and internal root sheath (described below).

### Structure of a Hair Follicle (Figs 22.5 and 22.6)

- In the centre of a hair follicle, there is a thin long filament, the hair shaft.
- The hair shaft is surrounded by two root sheaths: internal and external. Surrounding the external root sheath is the glassy membrane.



**Figure 22.5** Structure of sweat gland and hair follicle.



**Figure 22.6** Section of hair follicle in low magnification (H&E pencil drawing).



*Hair Shaft or Hair*

- Part of the hair shaft is in the centre of a hair follicle and the remaining part of it extends beyond the skin surface.
- It is derived from the bulb of the hair follicle and consists of the following three layers:
  - (a) In the innermost layer, the medulla forms the core of the hair shaft; cells in this layer show little keratinisation.
  - (b) Surrounding the medulla is the second layer, the cortex, which consists of highly keratinised cells.
  - (c) The third layer is cuticle, which consists of highly keratinised flat cells.
- The hair shaft is surrounded by internal and external root sheaths.

*Internal Root Sheath*

- It is the sheath that surrounds the hair shaft.
- It is derived from the bulb of the hair follicle and extends till the opening of the duct of the sebaceous gland into the hair follicle.
- Cells in this layer show little keratinisation. It is composed of inner cuticle, middle Huxley and outermost Henle's layers. Cuticle consists of keratinised flat cells. Huxley's layer consists of two to three layers of flat keratinised cells. Henle's layer is made up of a single cell layer.

*External Root Sheath*

- Outside the internal root sheath is the external root sheath.
- It is derived from epidermis.

*Glassy Membrane*

- It is present between the external root sheath and the connective tissue of dermis (Fig. 22.6).
- It is formed by thickening of basement membrane.

**Arrector Pili Muscle**

- A bundle of smooth muscles is associated with each hair follicle, known as arrector pili muscle. At one end this muscle is attached to the papillary layer of dermis, and the other end is attached to the hair follicle below the sebaceous gland (Fig. 22.1; PMG 22.4).
- Contraction of the muscle results in erection of the hair and produces gooseflesh.
- During contraction of the muscle, the sebaceous gland gets compressed and releases its secretions into the hair follicle through its duct.

**SEBACEOUS GLANDS**

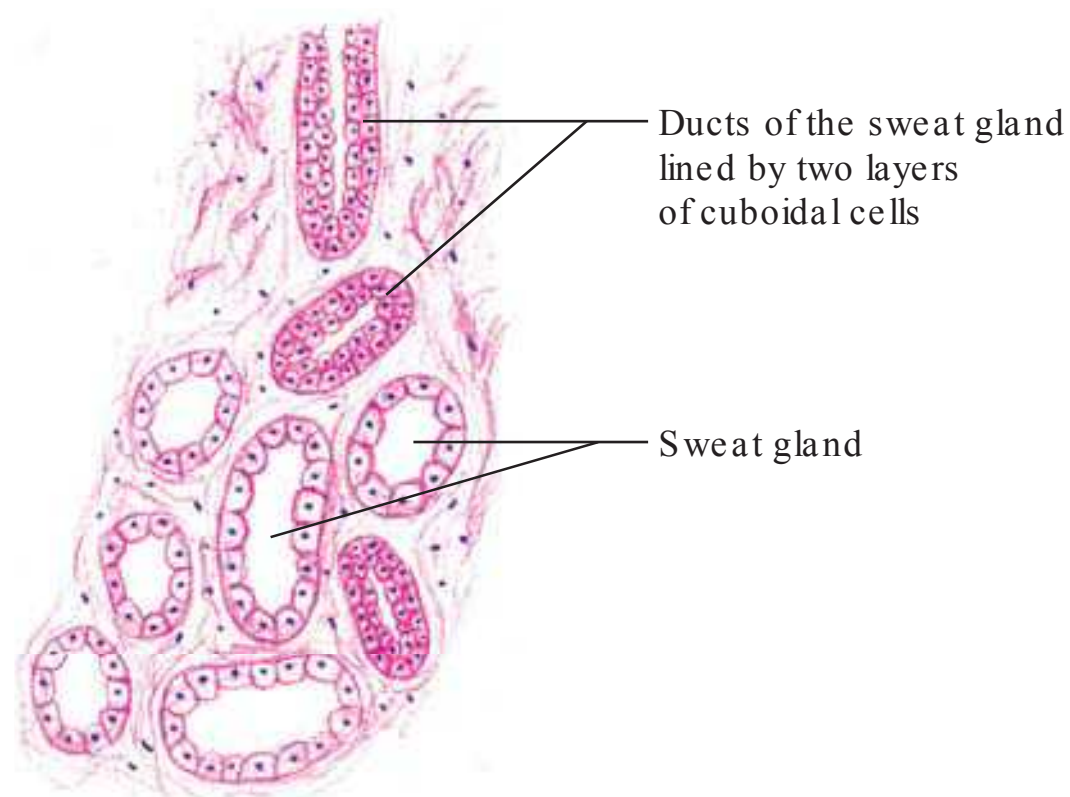
- Sebaceous glands are present only in the thin skin.
- They are branched acinar holocrine glands located in the dermis of thin skin. Each gland is associated with a hair follicle (Fig. 22.6; PMG 22.4).
- These glands produce oily secretion called sebum. They are more in the skin of the scalp and face, becoming functional at puberty.
- The gland consists of numerous acini (branched acinar gland) which open into a duct lined by stratified squamous epithelium, and this duct opens into the space around the hair shaft (Fig. 22.5).
- The hair follicle and associated muscle and sebaceous glands together are referred to as pilosebaceous apparatus.

## SWEAT GLANDS

There are two types of sweat glands: merocrine (or eccrine) and apocrine.

### Merocrine Sweat Glands

- These glands are present in the skin of the entire body except on the vermilion zone of the lips and glans penis.
- They are simple coiled tubular glands (Figs 22.2a, 22.5 and 22.7; PMG 22.1).
- The secretory unit is located deep in the dermis; it consists of a single layer of cuboidal cells resting on the basement membrane. There are two types of secretory cells in the secretory unit of this gland: dark and clear cells. Dark cells are more luminal in position than clear cells. Dark cells have secretory granules and numerous rough endoplasmic reticulum. Clear cells have abundant mitochondria and glycogen.



**Figure 22.7** Section of merocrine sweat gland in low magnification (H&E pencil drawing).

- Myoepithelial cells are present between the secretory cells and the basement membrane. Contraction of these cells helps in release of secretory product (sweat) from the secretory part of the gland.
- Ducts of the glands open on the skin surface. They stain more deeply than the secretory part, and are lined by two layers of cuboidal cells.
- These glands secrete watery fluid.

### Apocrine Sweat Glands

- These glands are present in the skin of axilla, perianal regions and areolae of the breast.
- They become functional at puberty. They secrete viscous fluid; bacteria present on the skin act on the secretion and produce odour.
- They are simple coiled tubular glands.
- The secretory unit is located in the dermis and consists of low cuboidal cells.
- Myoepithelial cells are similar to those in merocrine glands.
- Their duct opens in the hair follicle, just above the opening of the duct of the sebaceous gland. It is lined by two layers of cuboidal cells.
- The term apocrine is misleading as the secretion is merocrine type.



**NAILS (Fig. 22.8)**

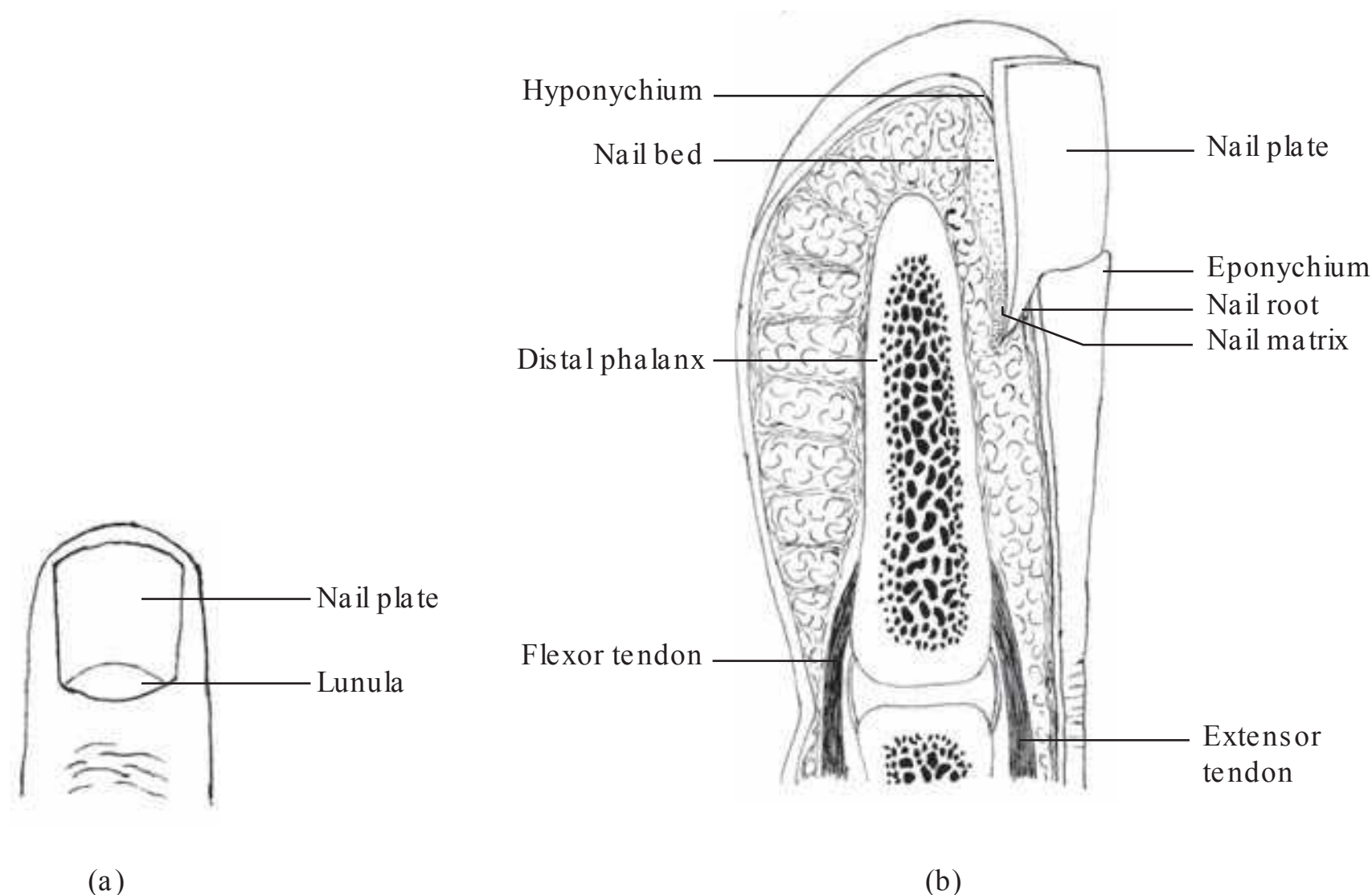
- Nails are hard keratinised plates present on the dorsal surface of the distal phalanx of fingers and toes.
- Each nail consists of two parts: nail plate and nail root.

**Nail Plate**

- The nail plate is the visible part of the nail; it rests on the nail bed, which is the epidermis of the skin. In the proximal part of the nail plate, there is a crescent-shaped opaque area known as lunula, which is more prominent in the thumb.
- The undersurface of the free edge of the nail plate is the fold of skin called hyponychium; this covers the nail bed.

**Nail Root**

- It is part of the nail which is proximal to the nail plate and it is covered with a fold of skin known as eponychium.
- Underneath the nail root is the nail matrix, and cells of the nail matrix proliferate and form the nail.



**Figure 22.8** Parts of nail (a) on gross appearance and (b) as seen in sagittal section.

## CLINICAL CORRELATES

**Vitiligo**

- It results from degeneration of melanocytes, causing depigmentation of skin. Treatment is phototherapy (UV light).

**Acne Vulgaris**

- Commonly referred to as pimples, it is a self-limiting disorder that occurs due to blockage of sebum outflow, resulting in small cysts.

**Malignant Melanoma**

- It is a cancer arising from the melanocytes.

KEYPOINTS

Types of Skin

- Thin
- Thick

Comparison of Thick and Thin Skin

Features	Thick skin (Fig. 22.2; PMG 22.2)	Thin skin (Fig. 22.1; PMG 22.1)
Thickness of epidermis	Thick (≈0.5 mm)	Thin (≈0.1 mm)
Layers of epidermis	All five	Stratum lucidum absent
Hairs	Absent	Present
Sebaceous glands	Absent	Present
Merocrine sweat glands	More	Less
Distribution	Palm and sole	All over the body except palm and sole

Parts of Skin (Fig. 22.2)

Part of skin	Layer	Components
Epidermis	Stratum germinativum	<ul style="list-style-type: none"><li>• Single layer of columnar or cuboidal-shaped keratinocytes over the basement membrane</li></ul>
	Stratum spinosum	<ul style="list-style-type: none"><li>• Several layers of keratinocytes</li><li>• Deeper layers—cells are polygonal with spherical nucleus; cells and their nuclei gradually flatten as they move towards the superficial layer</li><li>• Cells have cytoplasmic projections, and hence these cells are also called prickly cells</li></ul>
	Stratum granulosum	<ul style="list-style-type: none"><li>• Four to five layers of flattened cells</li><li>• These cells contain keratohyalin granules</li></ul>
	Stratum lucidum (only in thick skin)	<ul style="list-style-type: none"><li>• Appears as a narrow translucent layer and has several layers of flattened dead cells</li><li>• Nuclei and other cell organelles are not seen; cytoplasm has abundant keratin filaments</li></ul>
	Stratum corneum	<ul style="list-style-type: none"><li>• 15–20 layers of dead keratinised cells</li><li>• Cells are very flat, without cell organelles and nuclei</li></ul>
Dermis	Papillary (superficial layer)	<ul style="list-style-type: none"><li>• Consists of loose connective tissue</li><li>• Forms dermal papillae at the junction of epidermis, which interdigitate with downward projections of epidermis called epidermal ridges</li></ul>
	Reticular (deep layer)	<ul style="list-style-type: none"><li>• Reticular dermis is deep and consists of irregular dense connective tissue</li></ul>



Skin Appendages—Glands

Gland	Microscopic features
Sebaceous gland (Fig. 22.6; PMG 22.4)	<ul style="list-style-type: none"><li>• Located in the dermis of thin skin, associated with a hair follicle</li><li>• Branched acinar holocrine glands; their duct is lined by stratified squamous epithelium</li></ul>
Sweat gland (a) Merocrine (Figs 22.2a and 22.7; PMG 22.1)  (b) Apocrine	<ul style="list-style-type: none"><li>• Simple coiled tubular glands</li><li>• Secretory unit: Single layer of cuboidal cells over a basement membrane, myoepithelial cells</li><li>• Ducts: They open on the skin surface. They are lined by two layers of cuboidal cells</li></ul> <ul style="list-style-type: none"><li>• Simple coiled tubular glands</li><li>• Secretory unit: Low cuboidal cells, myoepithelial cells</li><li>• Ducts: They open in the hair follicle, just above the opening of the duct of sebaceous gland. They are lined by two layers of cuboidal cells</li></ul>

SELF-ASSESSMENT

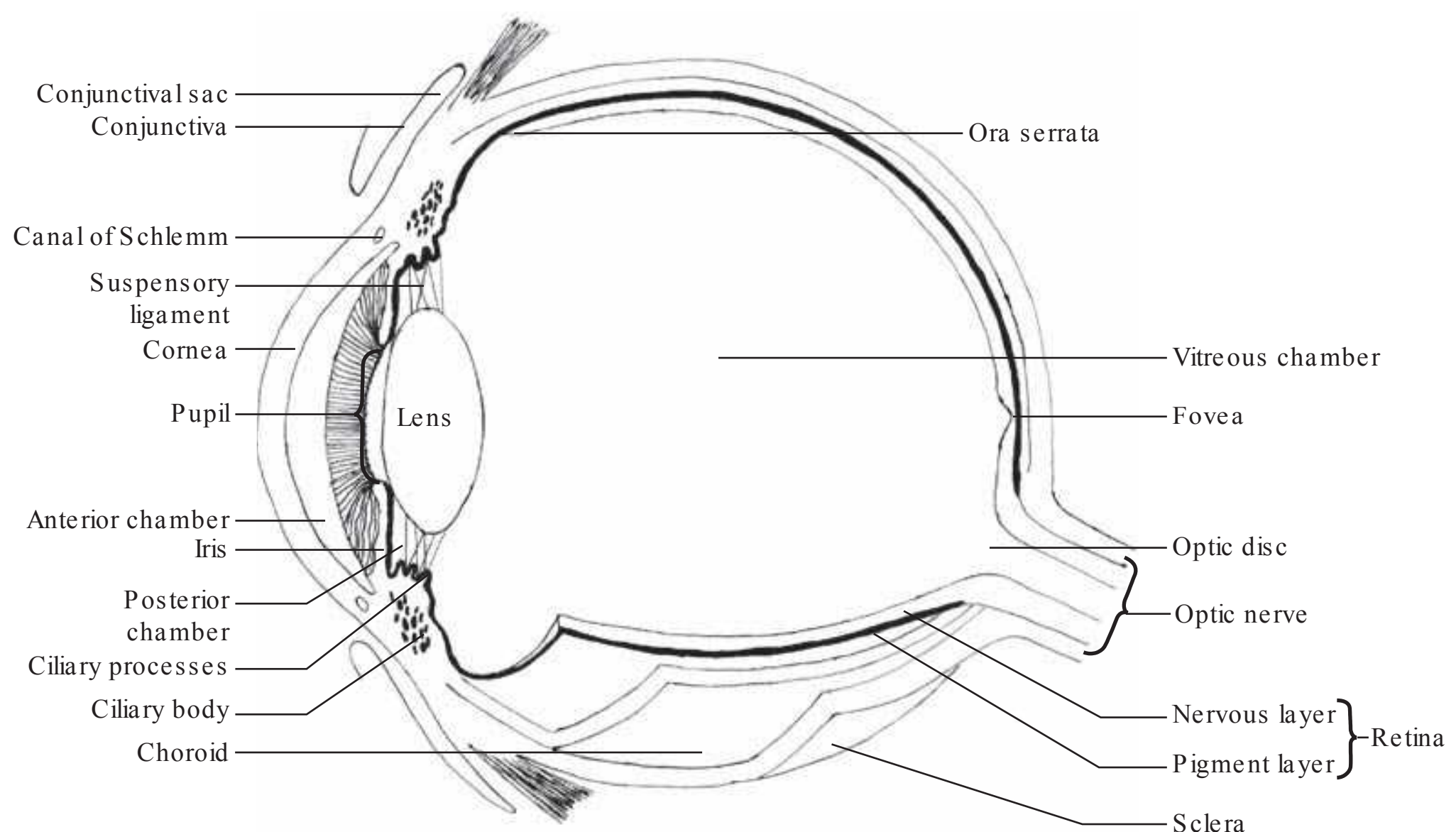
1. Name the different layers of epidermis.
2. Name the two layers of dermis. What are the histological differences between them?
3. Which are the different types of sweat glands? Mention their distribution in the body.
4. Compare the microscopic features of thick and thin skin.
5. What are melanocytes? Where are they located?

# Sense Organs

- Sensory organs have specialised cells, the receptors, which are responsible for providing information about the internal and external environment to the central nervous system. Receptors along with their supporting cells constitute a sense organ.
- There are five types of sensory modalities, namely vision, smell, taste, hearing and somatic sensations. Somatic sensations include touch, pressure, pain, proprioception and temperature.
- Taste and olfactory receptors have already been described in their respective systems. In this chapter, the microscopic structure of eye, ear and cutaneous receptors is discussed.

## EYE

- Eyes are the organ of sight; they are located in the bony orbit.
- The wall of an eye consists of three layers: outermost tunica fibrosa, middle tunica vasculosa and inner retina.
- Tunica fibrosa is subdivided into sclera and cornea (Fig. 23.1).



**Figure 23.1** Structure of an eyeball.



- Tunica vasculosa consists of three parts: choroid, ciliary body and iris (Fig. 23.1).
- The innermost tunic, the retina, consists of two layers: outer pigment layer and inner neural layer (Fig. 23.1).
- An eye has three chambers: anterior, posterior and vitreous (Fig. 23.1).
  - (a) The anterior chamber lies between the cornea and the iris.
  - (b) The posterior chamber lies between the iris and the lens.
  - (c) The vitreous chamber lies between the posterior surface of the lens and the neural retina.

### **TUNICA FIBROSA**

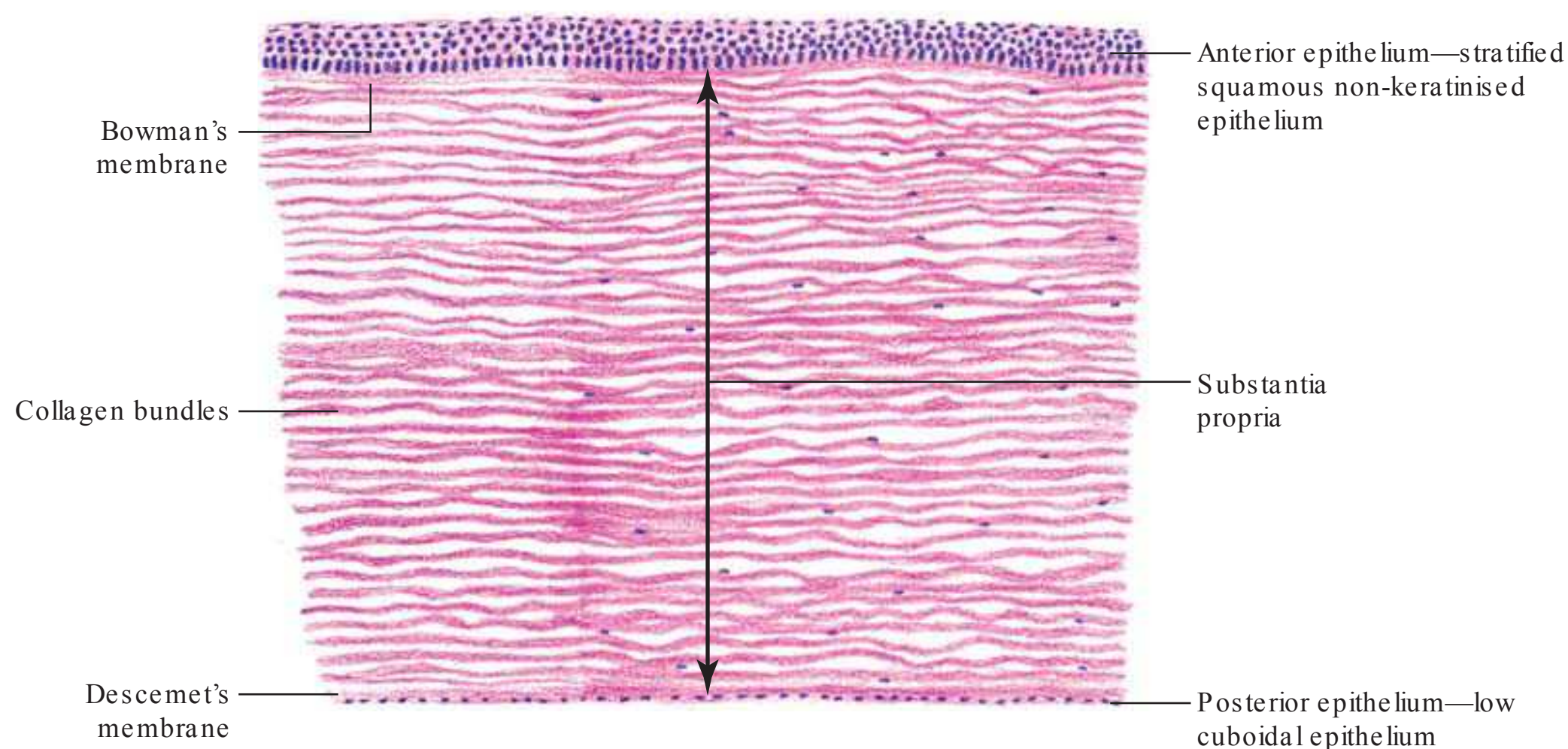
- Tunica fibrosa is subdivided into sclera and cornea.
- Cornea is a transparent layer and covers the anterior one-sixth of the eye.
- Sclera covers the posterior five-sixths of the eye and forms the 'white' of the eye. It consists of mainly dense fibrous connective tissue.
- The junction between the cornea and the sclera is called limbus.

### **Cornea**

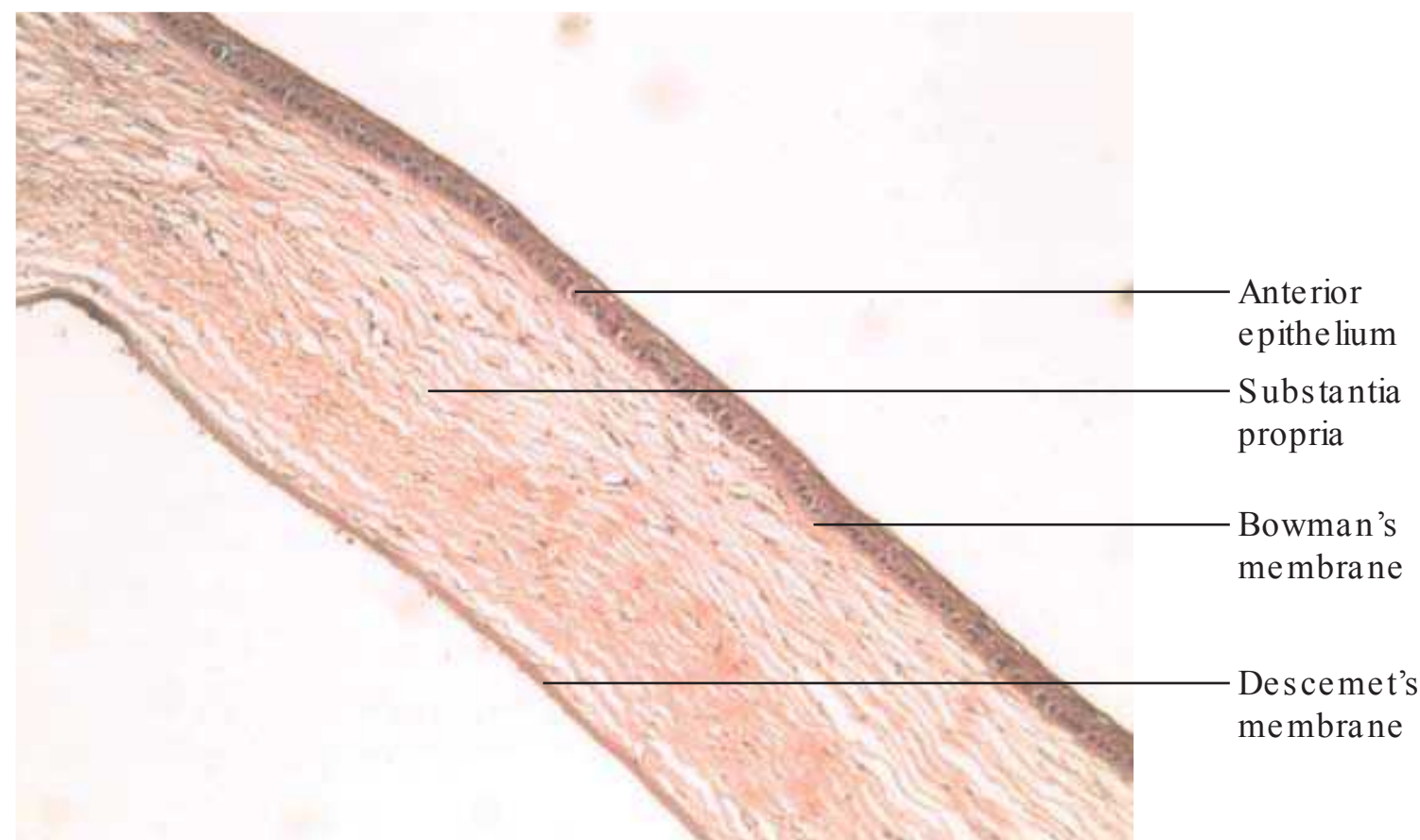
- Cornea is present in the anterior one-sixth of the eye.
- It is transparent, colourless and avascular.

### *Microscopic Features*

- It consists of the following five layers (from anterior to posterior) (Fig. 23.2; PMG 23.1):
  - (a) Anterior epithelium: It covers the outer surface of the cornea. It is four to five layers thick and consists of stratified squamous non-keratinised epithelium.
  - (b) Bowman's membrane (anterior limiting lamina): It is the thickened basement membrane on which the epithelium rests.
  - (c) Substantia propria (stroma): It forms the bulk of cornea and consists of several layers of collagen fibres; this layer also contains numerous fibroblasts. It lacks blood vessels and lymphatics; absence of these vessels makes cornea transplant successful.
  - (d) Descemet's membrane (posterior limiting membrane): It is the thickened basement membrane which supports the underlying posterior epithelium.
  - (e) Posterior epithelium (corneal endothelium): It is simple epithelium and cells are low cuboidal.



**Figure 23.2** Section of cornea in low magnification (H&E pencil drawing).



**PMG23.1** Cornea (H&E stain, X10).

### Sclera

- It provides protection and maintains the shape of the eye.
- It is pierced by blood vessels, nerves and optic nerve.

#### *Microscopic Features*

- It consists of the following three layers (from outside to inside):
  - (a) Episclera: It consists of loose connective tissue. The tendons of extraocular muscles pierce this layer and get attached to the middle layer of sclera, the stroma.
  - (b) Stroma: It consists of densely packed collagen fibre bundles and elastic fibres. The collagen fibre bundles are randomly arranged, and such arrangement of collagen makes the sclera opaque white.
  - (c) Lamina fusca: This is the innermost layer, which connects the sclera to choroid. It consists of loose connective tissue. Melanocytes are also present in this layer.

### TUNICA VASCULOSA

- It is also called uveal tract. It is vascular and pigmented.
- It consists of three parts: choroid, ciliary body and iris.

### Choroid

- It consists of loose connective tissue. Numerous melanocytes are present in it.
- Numerous blood vessels are present in the deep zone of choroid, which is called the choriocapillary layer.
- Between the choriocapillary layer and the pigment epithelium of retina is the Bruch's membrane. It consists of three layers—a layer of elastic fibres in the middle and layers of collagen fibres on both sides of it.

### Ciliary Body

- It is an extension of choroid between choroid and iris (Fig. 23.1).
- On the outer surface of the ciliary body is the sclera and on the inner surface is the vitreous chamber.
- The inner surface of the ciliary body is lined by two layers of cells—the outer cell layer is pigmented, whereas the inner cell layer (facing the posterior chamber) is non-pigmented. The cells of the inner layer secrete aqueous humour.



- The anterior part of the inner surface of the ciliary body has short processes towards the lens, known as ciliary processes (Fig. 23.1).
- Suspensory ligament of the lens extends from the ciliary processes to the capsule of the lens (Fig. 23.1). Ciliary muscles are smooth muscles present in the ciliary body, and they are attached to sclera. Contraction and relaxation of these muscles alter the convexity of the lens which is required for focusing on near and far objects.

### Iris

- It is the extension of the choroid as a thin circular disc, with a central aperture known as pupil, through which it controls the amount of light reaching the retina.
- It separates the anterior and posterior chambers of the eye, which communicate through pupil.

### Microscopic Features

- Iris consists of the following three layers:
  - (a) The anterior surface of the iris is covered by a discontinuous layer, which consists of pigmented cells and fibroblasts.
  - (b) Stroma: The stroma of the iris is composed of vascular loose connective tissue. Melanocytes and fibroblasts are also present. Two sets of smooth muscles, sphincter pupillae and dilator pupillae, are also present in the stroma. The size of the pupil is controlled by the contraction of these muscles. The sphincter pupillae muscle is arranged concentrically in the margin of the iris. It is supplied by parasympathetic fibres, and contraction of this muscle causes constriction of the pupil. Dilator pupillae muscle fibres are arranged in a radiating manner from papillary margin towards the periphery of the iris, and this muscle is innervated by sympathetic nerves. Contraction of this muscle increases the size of the pupil.
  - (c) A two-layered, thick pigment epithelium covers the posterior surface of the iris. These pigment cells absorb the light. The amount of pigment present determines the colour of the iris.

## RETINA

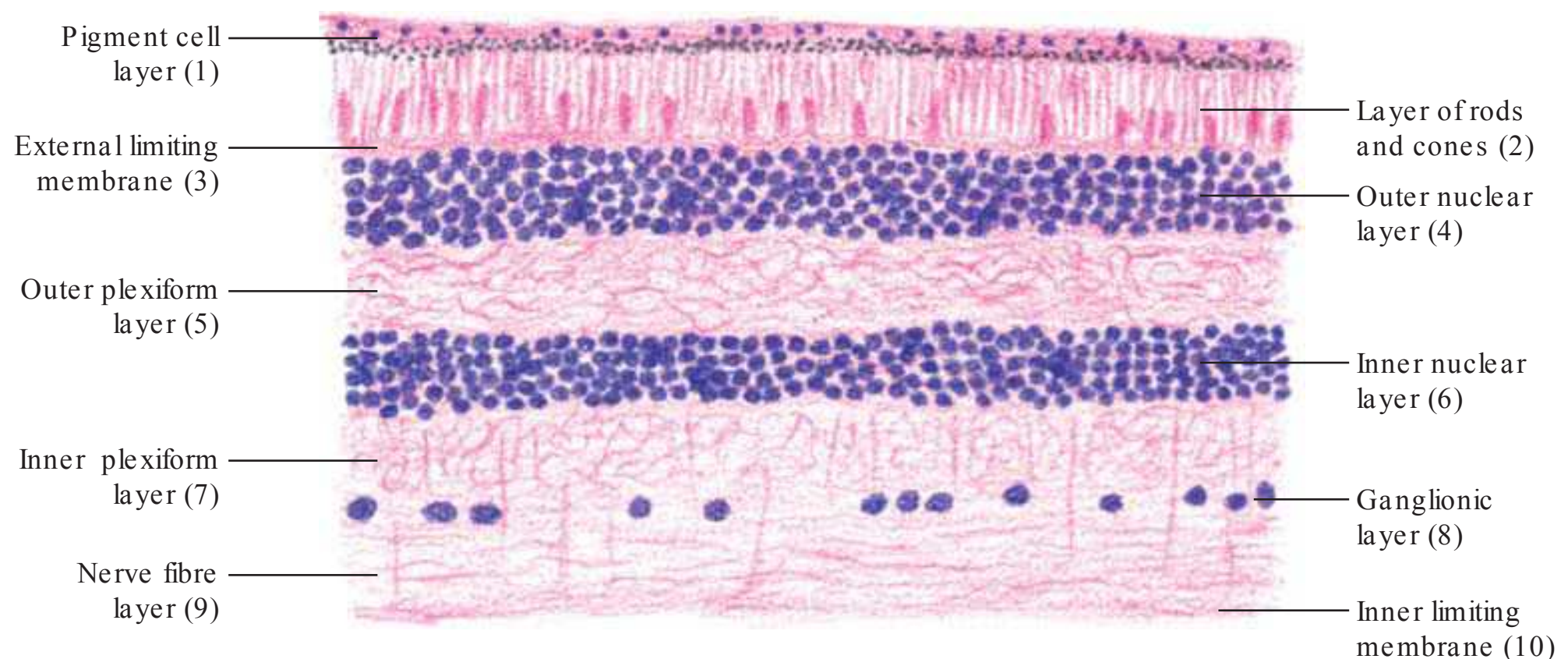
- The retina is the innermost of the three tunics.
- Developmentally, the retina consists of two layers: the outer pigment layer and the inner neural layer. The pigment layer develops from the outer wall of the optic cup and the neural layer from the inner wall of the optic cup. The two layers may get separated during the preparation of a histological slide.
- The nervous component ends at the ora serrata (Fig. 23.1), which is located at the periphery of the ciliary body. The pigment layer of the retina extends beyond ora serrata, over the ciliary body and iris.

### Microscopic Features

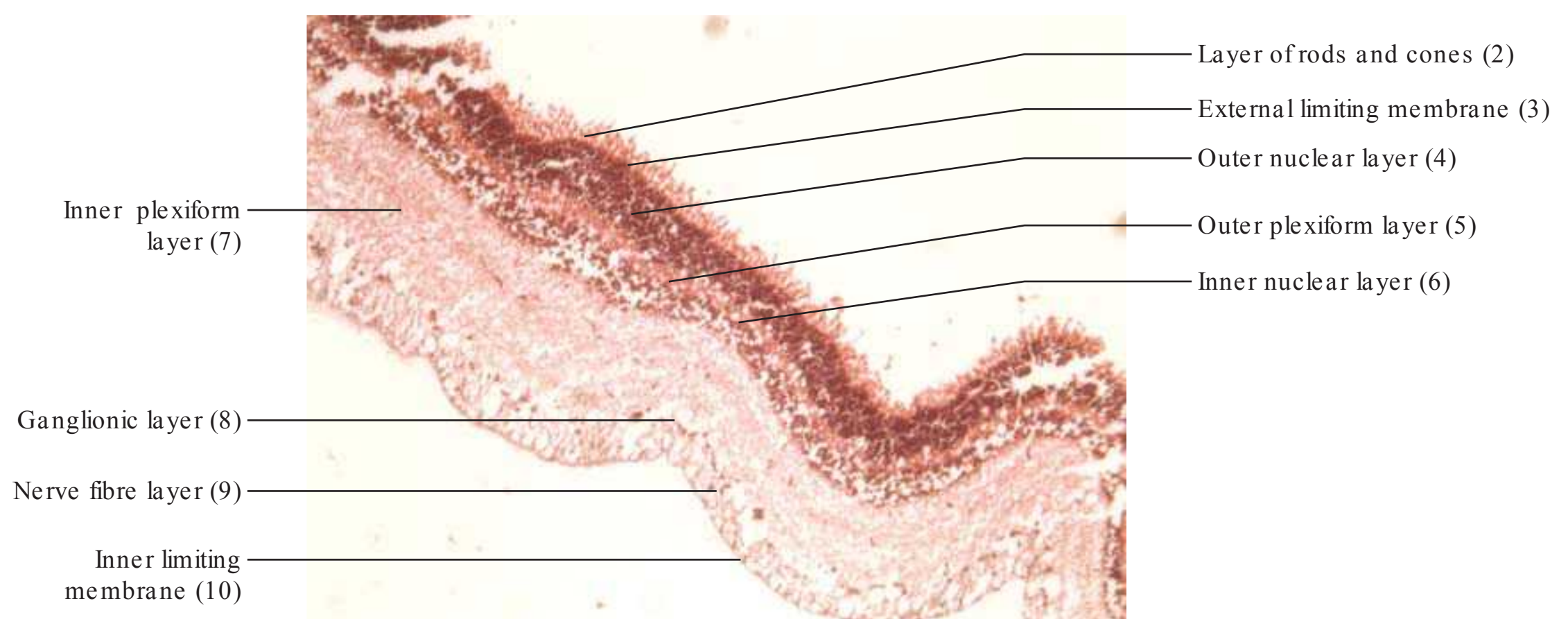
- Histologically, the retina consists of 10 layers (Figs 23.3 and 23.4; PMG 23.2)—the first layer is the pigment cell layer and the remaining layers constitute the neural layer of the retina. From outside inwards, the 10 layers are as follows:
  - (a) Pigment cell layer: It consists of a single layer of cuboidal cells resting on a thick basement membrane (Bruch's membrane). These cells contain melanin granules. This layer performs the following functions:
    - (i) It absorbs and prevents reflection of light that has passed through the neural layers of the retina.
    - (ii) The pigment cells phagocytose the shed membranous discs of the outer segment of rods and cones (described under the section 'Photoreceptors').
    - (iii) These cells also produce melanin.
  - (b) Layer of rods and cones: These are the photoreceptors, and they pass through the external limiting membrane.



- (c) External limiting membrane: It is a sieve-like membrane, formed by glial cells known as Muller cells.
- (d) Outer nuclear layer: This layer consists of nuclei of photoreceptors.
- (e) Outer plexiform layer: In this layer, the axons of rods and cones synapse with the dendrites of bipolar cells. Bipolar cells connect rods and cones to the ganglion cells.
- (f) Inner nuclear layer: It contains nuclei of bipolar cells, Muller cells, horizontal cells and amacrine cells. Horizontal cells establish contact between different photoreceptors in the outer plexiform layer. Amacrine cells connect different ganglion cells and bipolar neurons to each other in the inner plexiform layer.
- (g) Inner plexiform layer: In this layer, the axons of bipolar cells synapse with the dendrites of ganglion cells.
- (h) Ganglionic cell layer: This layer consists of large cell bodies of ganglion cells.
- (i) Nerve fibre layer: Axons of the ganglion cells travel in this layer towards the optic disc.
- (j) Inner limiting membrane: This layer consists of the processes of Muller cells.

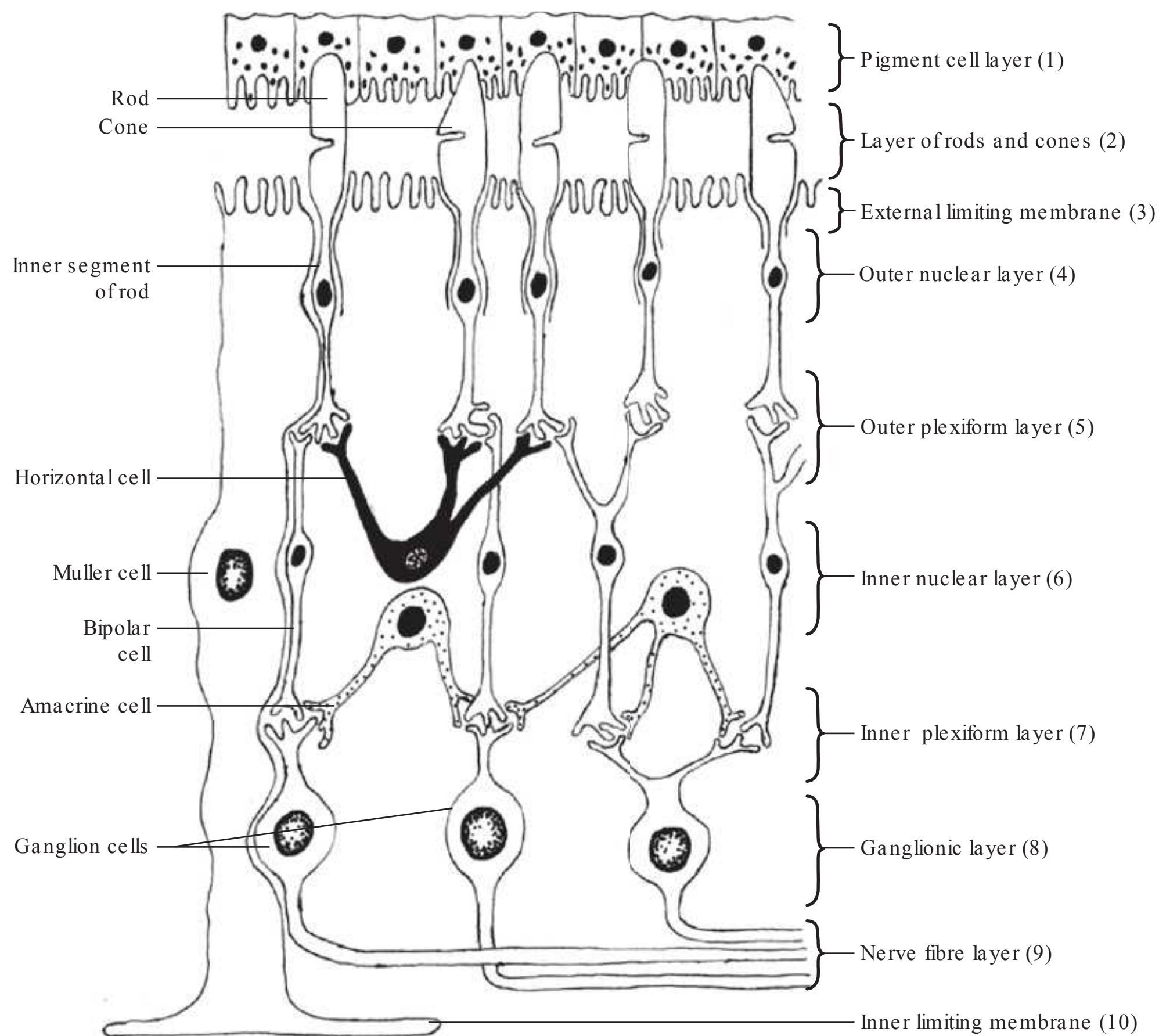


**Figure 23.3** Section of retina in low magnification (H&E pencil drawing). The numbers in brackets indicate the sequence of the layers.



**PMG 23.2** Retina. Note that the pigment cell layer is not seen, as it gets separated from the nervous layer of the retina during histological preparation (H&E stain, X10). The numbers in brackets indicate the sequence of the layers.





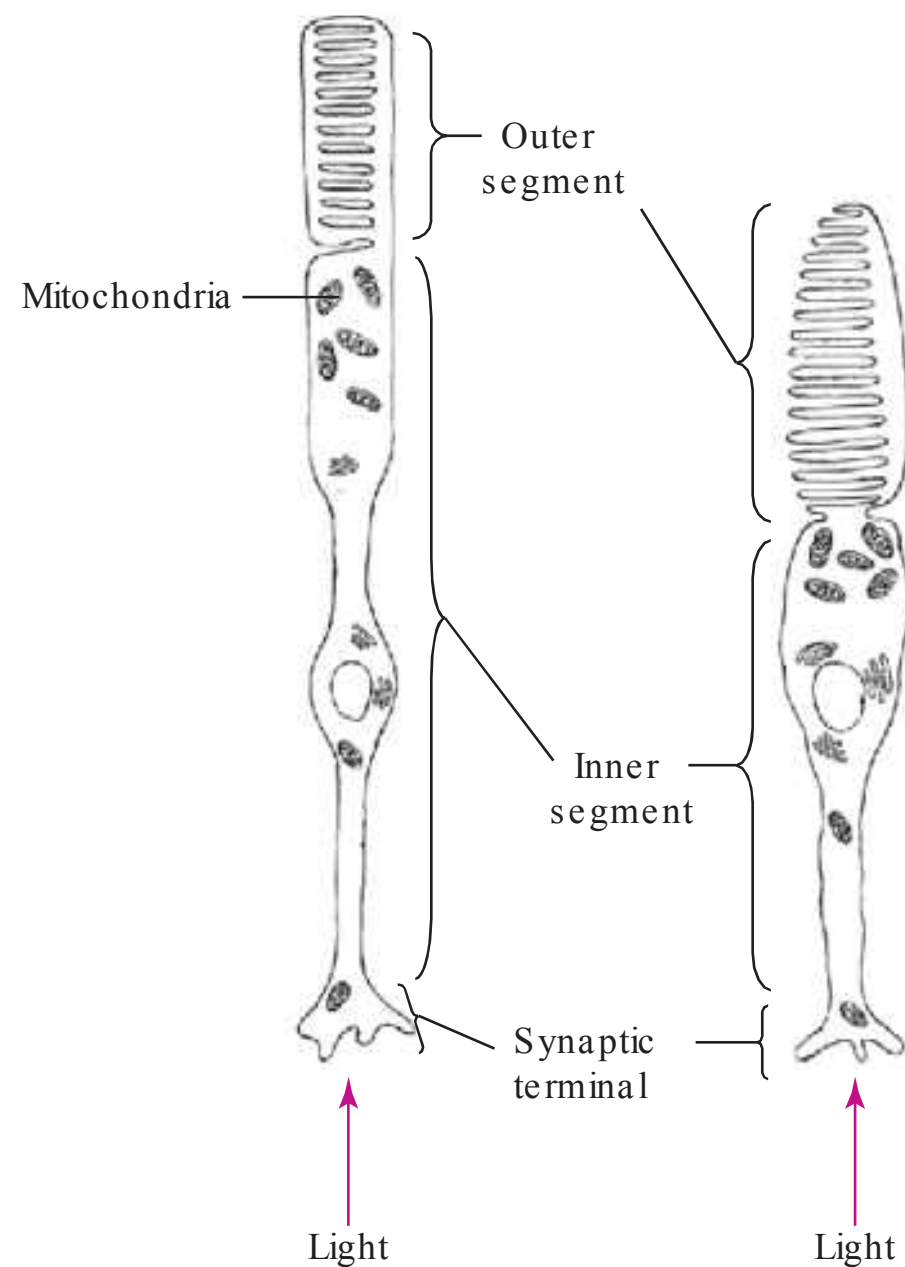
**Figure 23.4** Schematic diagram showing the layers of retina. The numbers in brackets indicate the sequence of the layers.

### Photoreceptors

- There are about 120 million rods and 6 million cones in each human eye.
- Rods are sensitive to dim light, whereas cones are sensitive to bright light. Cones provide colour vision and better visual acuity.
- Each photoreceptor has an outer segment and an inner segment (Fig. 23.5), connected by a connecting stalk, and a synaptic terminal which synapses with bipolar cells.
- The outer segment is cylindrical in rods and conical in cones. The outer segment contains stacks of membrane-bound discs containing photosensitive material; in rods the photosensitive material is rhodopsin (visual purple) and in cones it is iodopsin.
- In rods discs are independent, without any continuity with the adjacent discs, whereas in cones discs are not completely separate; the plasma membrane is continuous.
- The old discs are renewed by addition of new discs at the base of the outer segment. The old discs are shed from the tips of the outer segment and they are phagocytosed by the pigment cells.

### Bipolar Cells (Fig. 23.4)

- The cell bodies of bipolar cells are located in the inner nuclear layer of the retina.
- Their dendrites synapse with the synaptic terminals of photoreceptor cells in the outer plexiform layer.



**Figure 23.5** Photoreceptors: rod (left) and cone (right).

- Their axon synapses with ganglion cells in the inner plexiform layer.
- They transmit the impulse generated by photoreceptors to the ganglion cells.

#### *Ganglion Cells* (Figs 23.3 and 23.4; PMG 23.2)

- Ganglion cells have large cell bodies.
- Dendrites of these cells synapse with bipolar neurons.
- Axons of these cells travel towards the optic disc in the nerve fibre layer of the retina.
- At the optic disc, all the axons of ganglion cells assemble to form optic nerve.

#### *Other Nerve Cells*

- The cell bodies of horizontal cells are located in the inner nuclear layer (Fig. 23.4). Their dendrites and axons extend into the outer plexiform layer and synapse with the photoreceptors.
- The cell bodies of the amacrine cells are located in the inner nuclear layer (Fig. 23.4). Their processes extend into the inner plexiform layer and connect different ganglion cells and bipolar neurons to each other.

#### *Muller Cells*

- These are glial cells, which serve as supporting cells for the nerve cells of the retina.
- The cell bodies of Muller cells are in the inner nuclear layer (Fig. 23.4). The processes of these cells occupy the extracellular space of the retina.
- The outer processes of these cells extend till the inner segment of the photoreceptors, and here similar processes of adjacent Muller cells are held together by zonula adherens to form the outer limiting membrane.
- The inner processes of these cells and their basal lamina together form the inner limiting membrane.



*Fovea Centralis* (Fig. 23.1)

- At the posterior pole (central point on the maximal convexity of the posterior curvature of the eyeball) of the eye, the retina has a yellow pigmented spot known as yellow spot or macula lutea, and in the centre of the yellow spot is a shallow depression known as fovea centralis.
- Fovea centralis is a rod-free region of the retina and the cones are densely packed. Visual acuity is greatest in this region.

*Optic Disc* (Fig. 23.1)

- The optic disc is a circular area located 1 mm above and 3 mm nasal to the posterior pole (Fig. 23.1).
- At the optic disc, all retinal layers terminate except the axons of ganglion cells, which form optic nerve.
- Since there are no rods and cones in this area, it is insensitive to light, and hence it is also called blind spot.

**REFRACTIVE MEDIA OF THE EYE**

The refractive media of the eye include the cornea, the aqueous humour, the crystalline lens and the vitreous body. Cornea has already been described.

**Aqueous Humour**

- The anterior and posterior chambers of the eye are filled with a watery fluid called aqueous humour.
- It is produced by the cells lining the ciliary body. It is secreted into the posterior chamber of the eye, and from the posterior chamber it goes through the pupil to the anterior chamber.
- From the anterior chamber, it enters the canal of Schlemm, and finally into the veins present in the sclera.
- It provides nutrition to the cornea and lens and helps in maintaining the intraocular pressure.

**Lens**

- The lens is a transparent, biconvex, flexible mass located between the iris and the vitreous body (Fig. 23.1).
- It is held in its position through the zonular fibres of the suspensory ligament of lens, which are attached to the ciliary processes (Fig. 23.1).
- It has two surfaces—the posterior surface is more convex than the anterior surface.

*Structure of the Lens*

- It is composed of lens capsule, anterior epithelium and lens fibres.
- A capsule of connective tissue covers the entire lens.
- Underneath the capsule, on the anterior surface of the lens is the anterior epithelium of lens, which consists of a single layer of cuboidal cells. These cells have gap junctions, and they elongate and differentiate into lens fibres.
- Lens fibres make the bulk of the lens and they are formed throughout life. New lens fibres are at the periphery, and the central hard part of the lens, known as nucleus of the lens, contains old lens fibres. The mature fibres contain crystalline protein, and they lack cell organelles and nuclei.

**Vitreous Body**

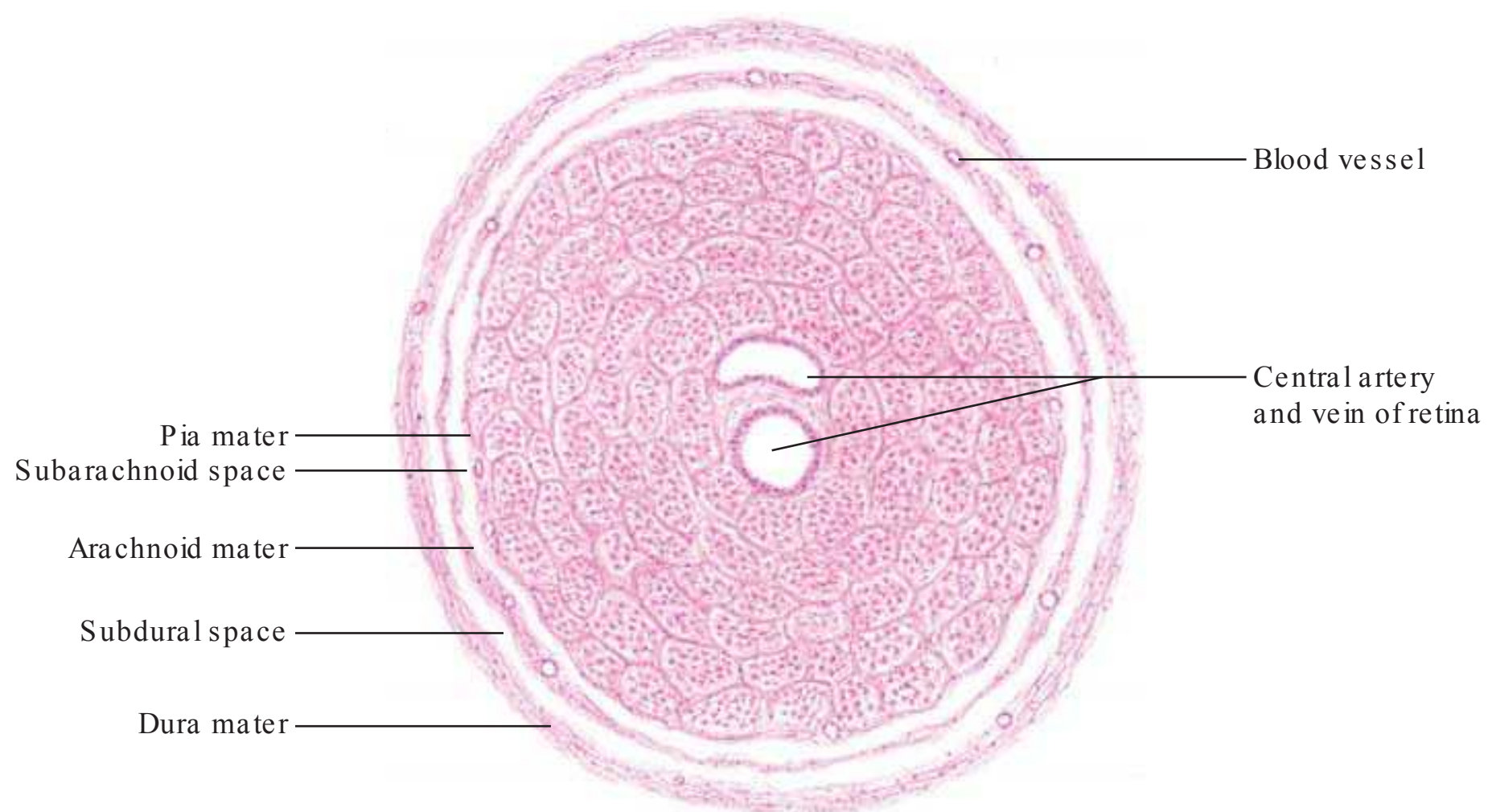
- The vitreous body consists of a gelatinous substance present in the vitreous chamber.

## STRUCTURES ASSOCIATED WITH EYES

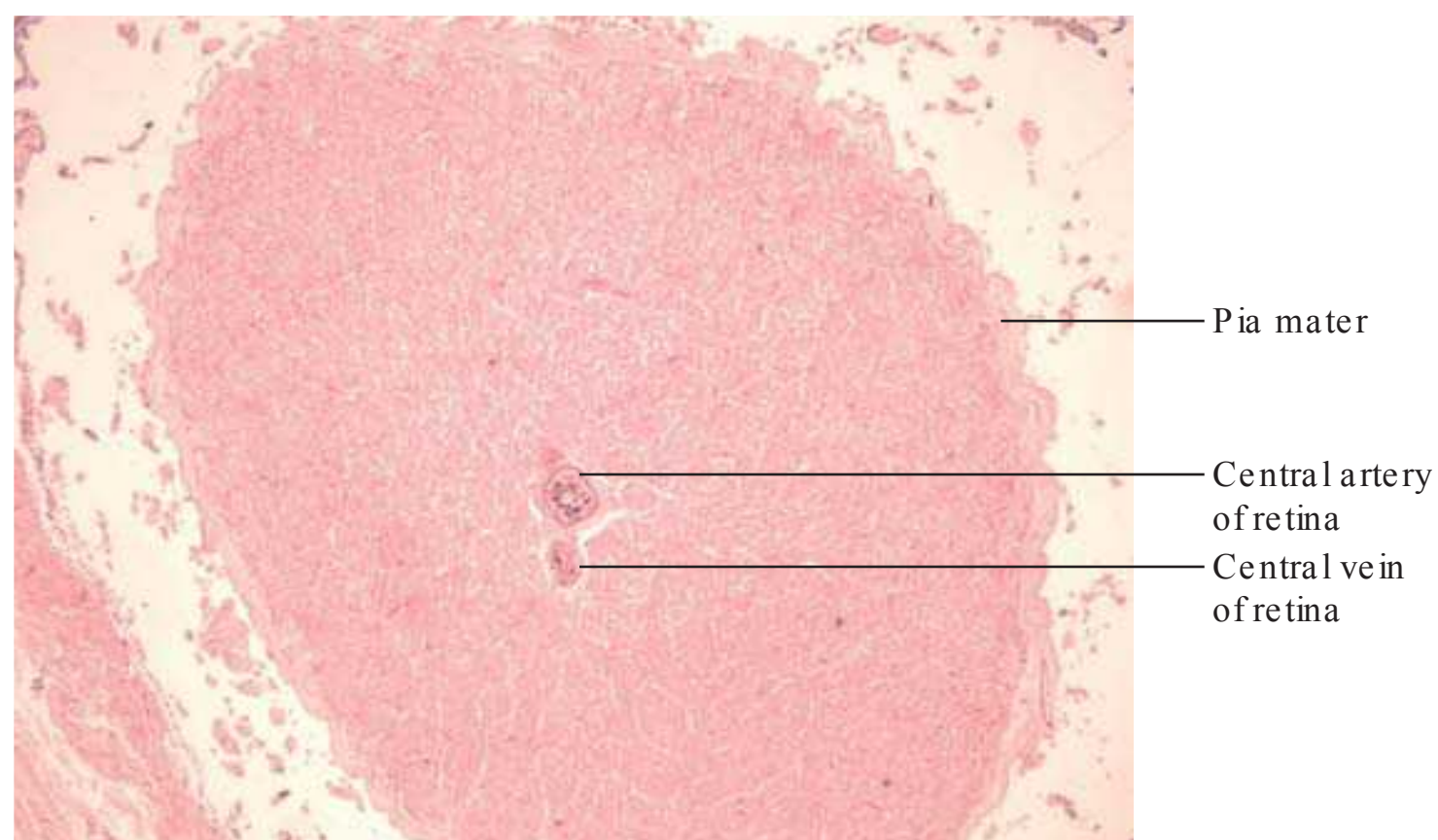
Optic nerve, eyelids, conjunctiva and lacrimal apparatus are discussed in this section.

### OPTIC NERVE

- Developmentally, it is an outgrowth from the brain.
- It contains fibres that originate from the ganglionic cell layer of the retina.
- It is covered by three sheaths: the outermost is dura mater, the middle is arachnoid mater and the innermost is pia mater (Fig. 23.6).
- From the pia mater, septa arise and enter the nerve and form numerous fascicles.
- In the centre are the central artery and vein of the retina (Fig. 23.6; PMG 23.3).



**Figure 23.6** Transverse section of optic nerve (H&E pencil drawing).



**PMG 23.3** Optic nerve (H&E stain, X5).

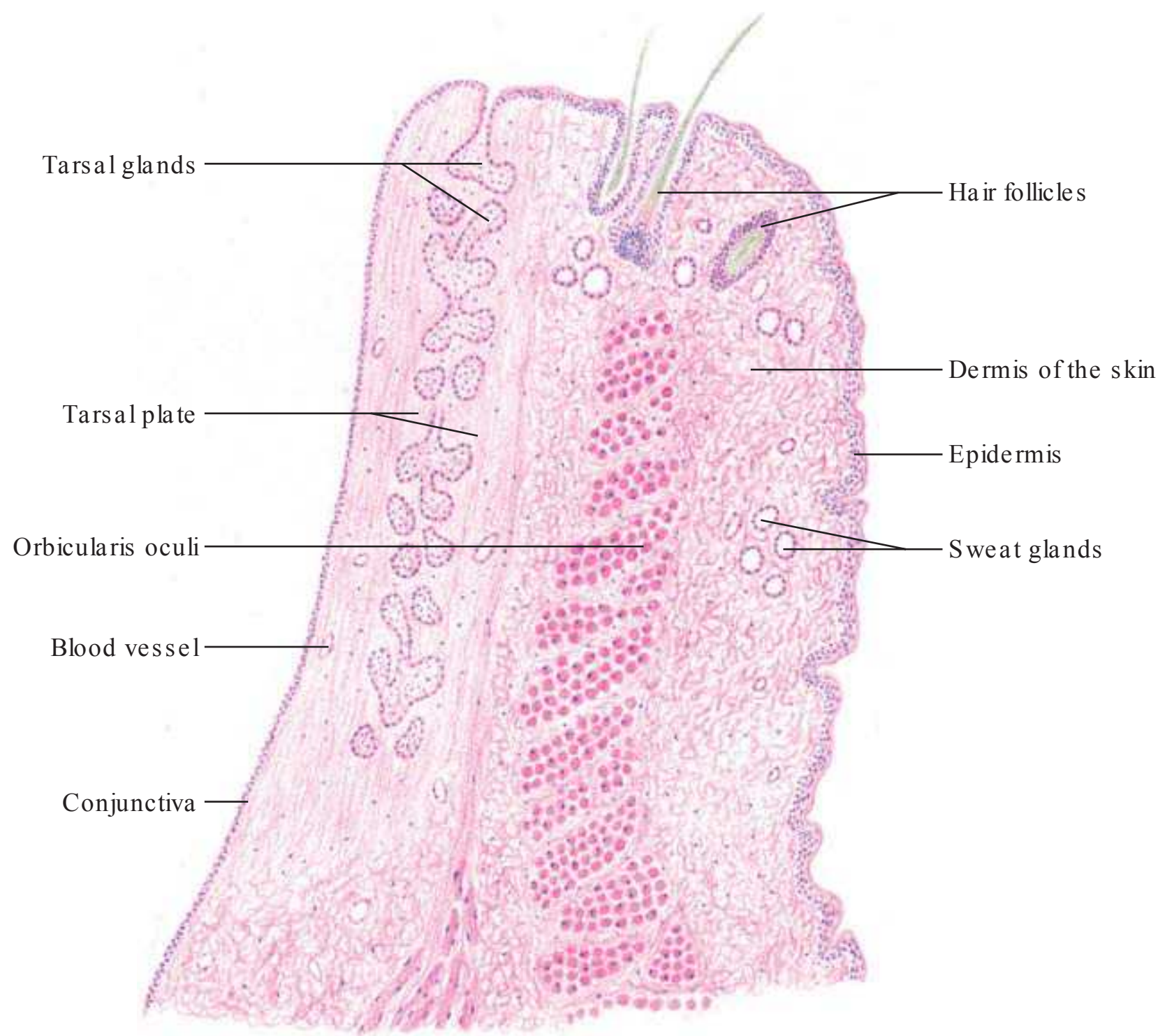


## EYELIDS

- Eyelids are movable skin folds. They provide protection to the eyes and keep the cornea clean and moist.

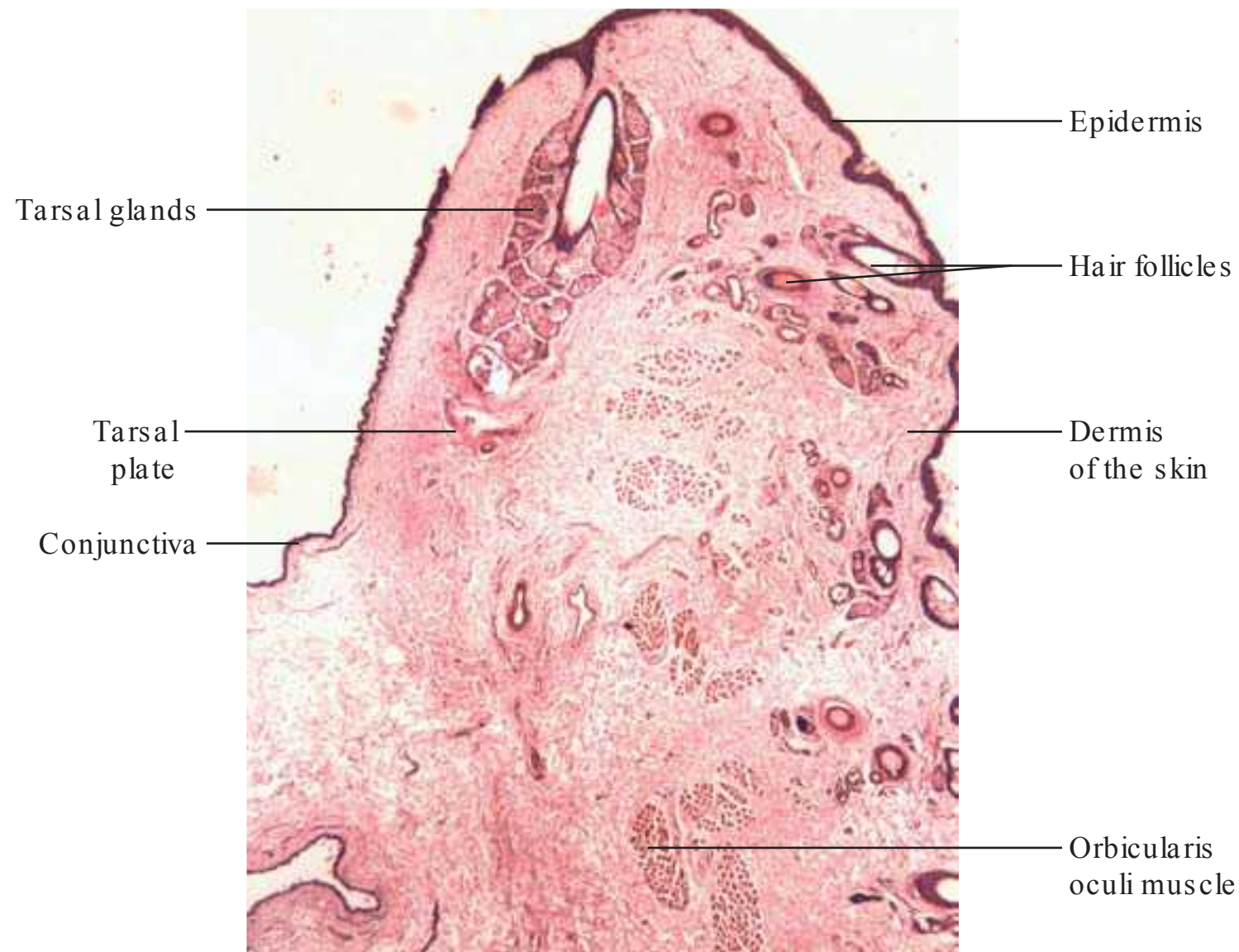
### Structure of an Eyelid

- From the anterior (external) surface to the posterior surface (facing the eyeball), the eyelid consists of the following layers (Fig. 23.7; PMG 23.4 and 23.5):
  - (a) Skin
  - (b) Muscle layer
  - (c) Tarsal plate
  - (d) Conjunctiva
- The anterior (external) surface of the eyelid is covered with skin.
- The skin covering the anterior surface is hairless except along the margins of the lid, where three to four rows of hairs, the eyelashes, are present. Modified apocrine sweat glands, the glands of Moll, and the sebaceous glands of Zeis are associated with each eyelash.
- Underneath the skin is a muscle layer which consists of orbicularis oculi and levator palpebrae muscle.
- The tarsal plate is a layer of dense connective tissue. It provides support to the eyelid. Numerous sebaceous glands are embedded in the tarsal plate, and these glands are known as tarsal glands or Meibomian glands. The ducts of these glands open on the free margin of the eyelid. The oily secretion of the tarsal gland forms a thin layer over the tear film and slows down its evaporation.
- The posterior surface (facing the eyeball) is covered with conjunctiva, which consists of stratified columnar or cuboidal epithelium.

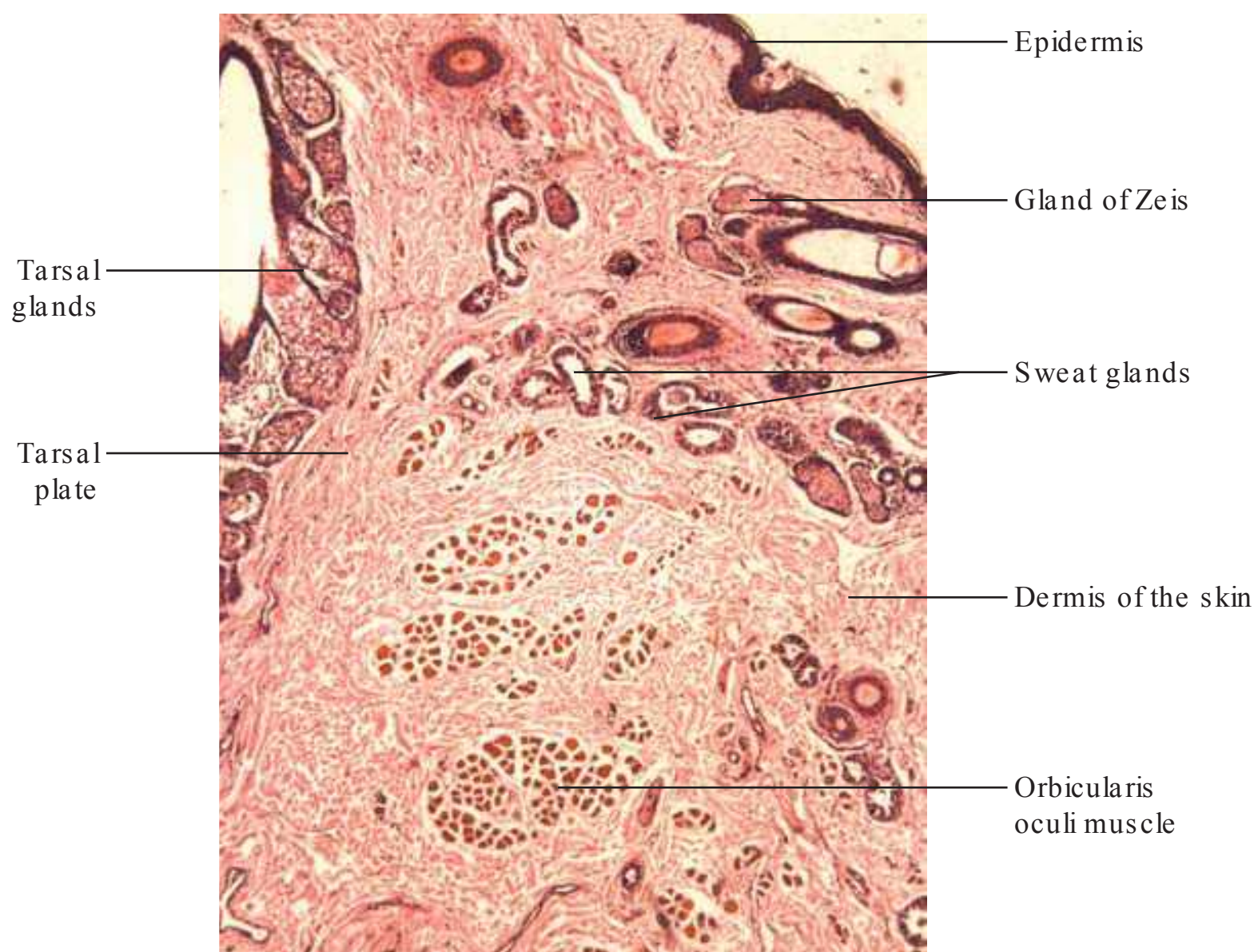


**Figure 23.7** Section of eyelid in low magnification (H&E pencil drawing).





**PMG 23.4** Eyelid (H&E stain, X2.5).



**PMG 23.5** Eyelid (H&E stain, X5).

## CONJUNCTIVA

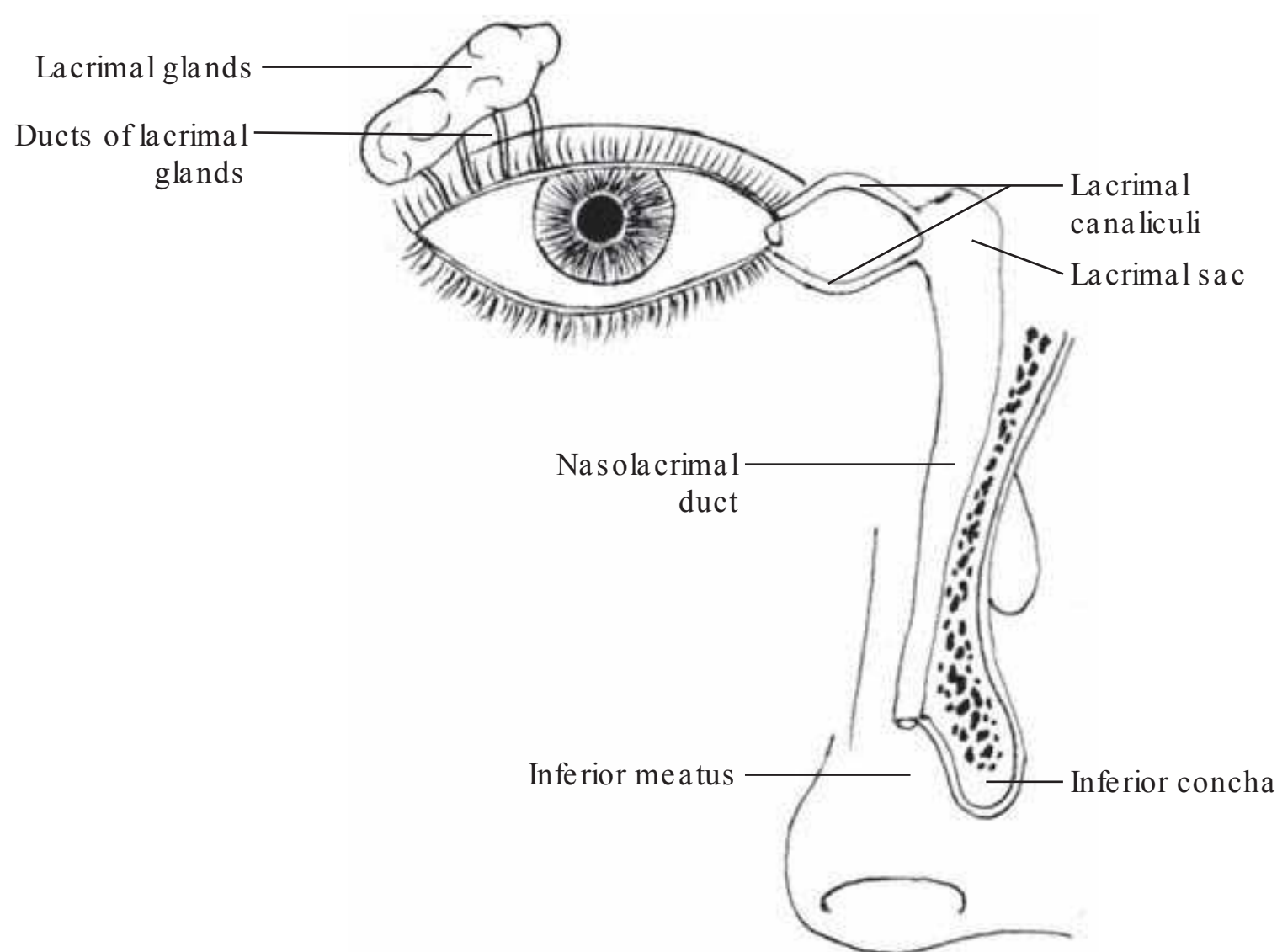
- Conjunctiva is a thin, transparent membrane and consists of two parts: bulbar and palpebral conjunctiva.
- The palpebral conjunctiva lines the inner surface of the eyelid and is reflected onto the sclera as bulbar conjunctiva, which covers the sclera up to the margin of the cornea (Fig. 23.1). The line of reflection is known as fornix (superior and inferior fornices in the respective eyelids).



- The space between the bulbar and palpebral conjunctivas is called a conjunctival sac (Fig. 23.1).
- Conjunctiva consists of stratified columnar epithelium. Numerous goblet cells are present in the epithelium. The epithelium rests on lamina propria which is composed of loose connective tissue.

### LACRIMAL APPARATUS

- The lacrimal apparatus consists of lacrimal gland, lacrimal canaliculi, lacrimal sac and nasolacrimal duct (Fig. 23.8).
- The secretions of the lacrimal gland reach the conjunctival sac through its ducts which open into the lateral part of the superior fornix.
- The tear enters the lacrimal canaliculus; from the lacrimal canaliculus the tear enters into the lacrimal sac, and from the lacrimal sac it drains into the inferior meatus of the nose through the nasolacrimal duct (Fig. 23.8).



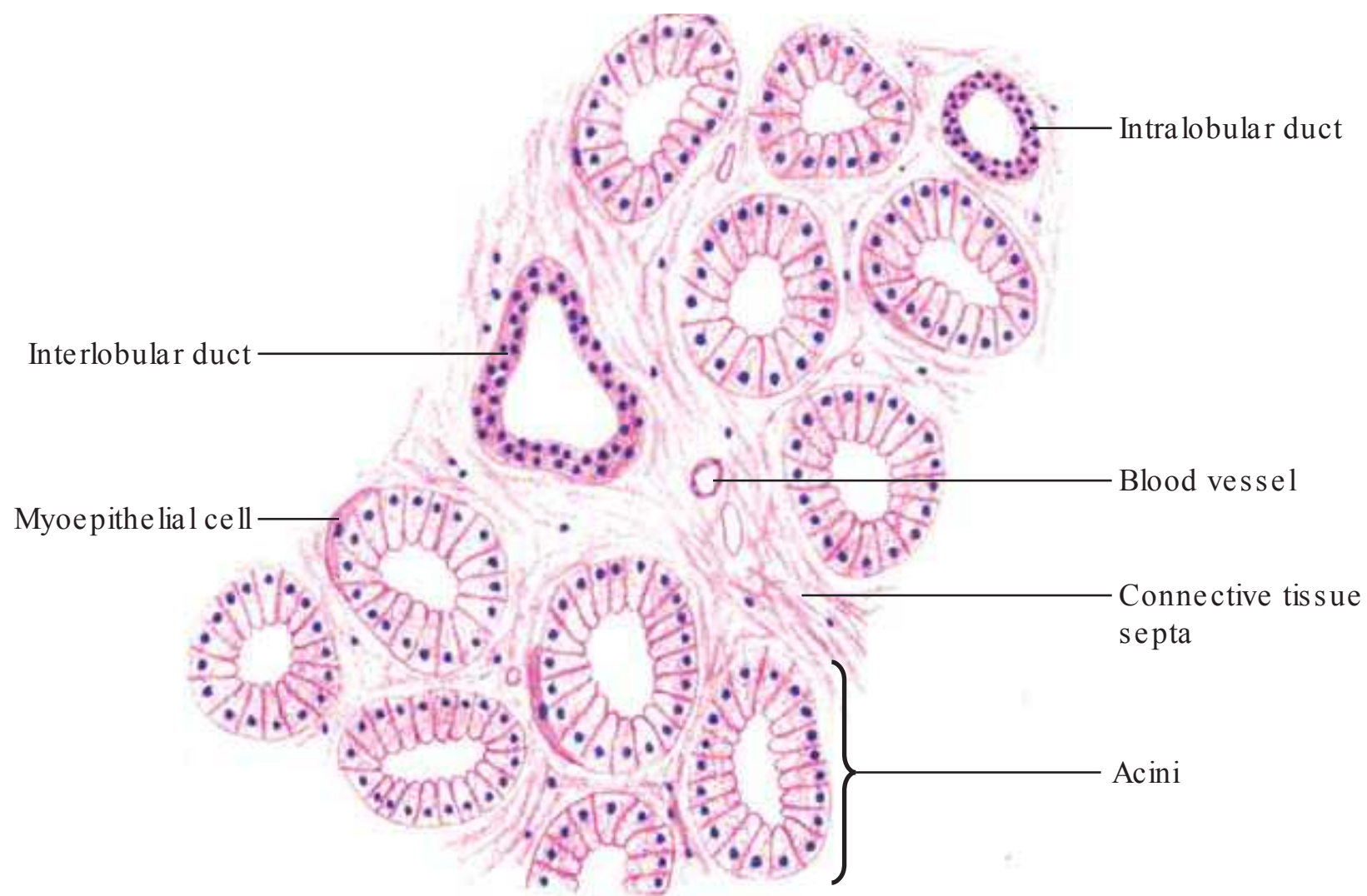
**Figure 23.8** Lacrimal apparatus of the right eye.

### Lacrimal Gland

- The lacrimal gland is located in the anterolateral part of the roof of each orbit (Fig. 23.8).
- It produces clear watery fluid, the tear. Tear is rich in electrolytes; it also contains lysozyme, an enzyme which has antibacterial action.

### Microscopic Structure (Fig. 23.9)

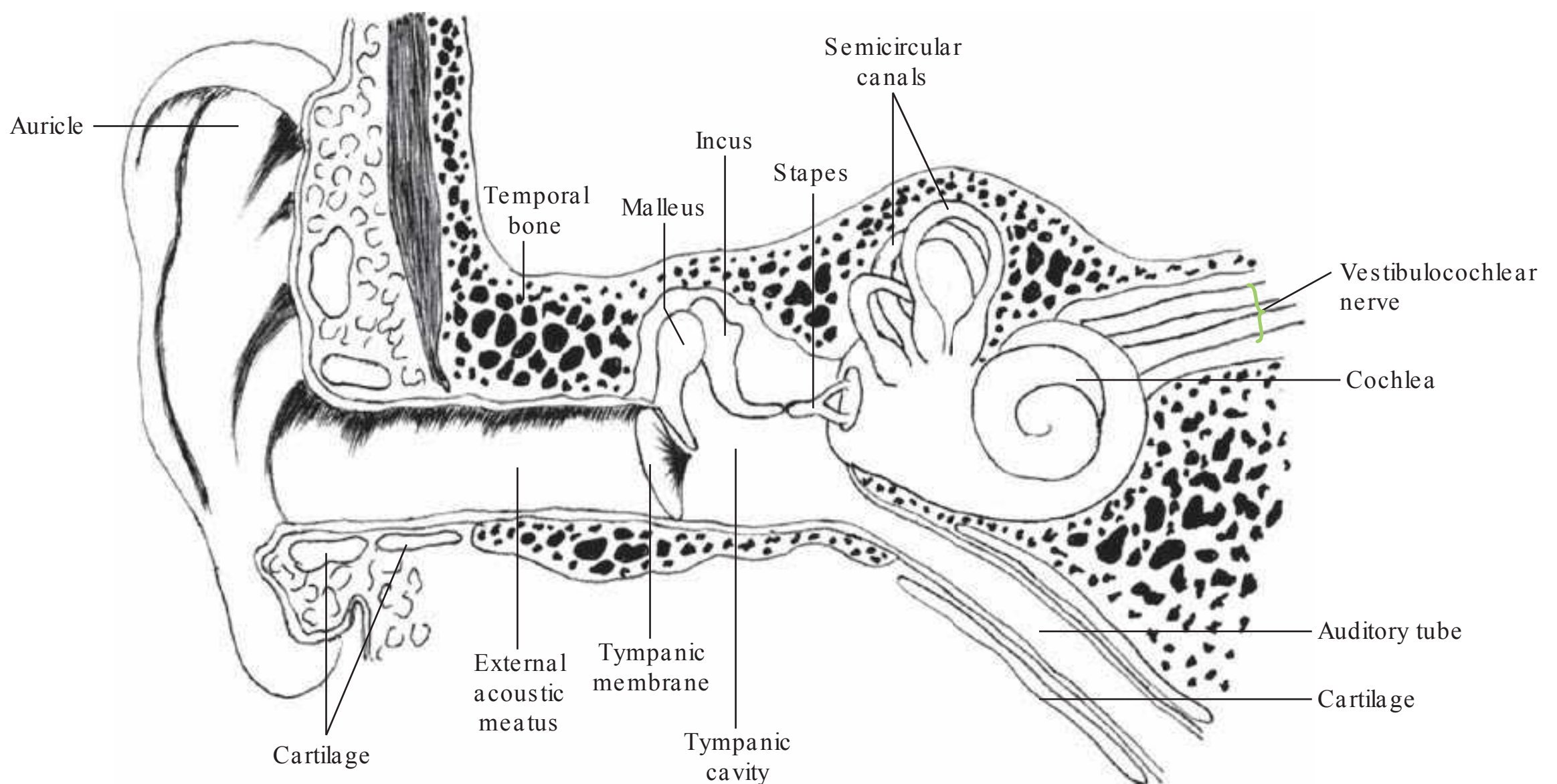
- The gland has several lobules separated by connective tissue.
- It is a compound tubuloacinar gland. The acini are lined by columnar cells.
- Myoepithelial cells are present between the glandular epithelium and the basement membrane.



**Figure 23.9** Section of the lacrimal gland in low magnification (H&E pencil drawing).

## EAR

- The ear is an organ specialised for hearing and equilibrium. It consists of three parts: external, middle and internal ear (Fig. 23.10).
- The external ear receives the sound waves from the external environment. The sound waves are intensified in the middle ear and passed to the inner ear.
- The inner ear has the receptors for hearing and equilibrium.



**Figure 23.10** Parts of ear—external, middle and internal.



## **EXTERNAL EAR**

- The external ear consists of pinna or auricle and external auditory meatus (Fig. 23.10).
- The pinna projects from the lateral aspect of the head. The entire pinna, except the lobule, consists of a plate of elastic cartilage covered with thin skin. The lobule, however, consists of fibrofatty tissue.
- The cartilage of pinna is continuous with the cartilage in the outer third of the external auditory meatus. The inner two-thirds of the external auditory meatus are bony (temporal bone).
- The external auditory meatus is lined by thin skin. It contains numerous sebaceous glands and modified sweat glands known as ceruminous glands. Ceruminous glands secrete ear wax.

## **TYMPANIC MEMBRANE**

- The tympanic membrane separates the external ear from the middle ear (Fig. 23.10).
- From outside to inside, it consists of three layers: the outer layer is made up of skin which is continuous with the skin of the external auditory meatus, the middle layer consists of dense fibrous connective tissue and the inner layer is formed by simple cuboidal epithelium.
- It transmits sound waves from the external ear to the middle ear.

## **MIDDLE EAR**

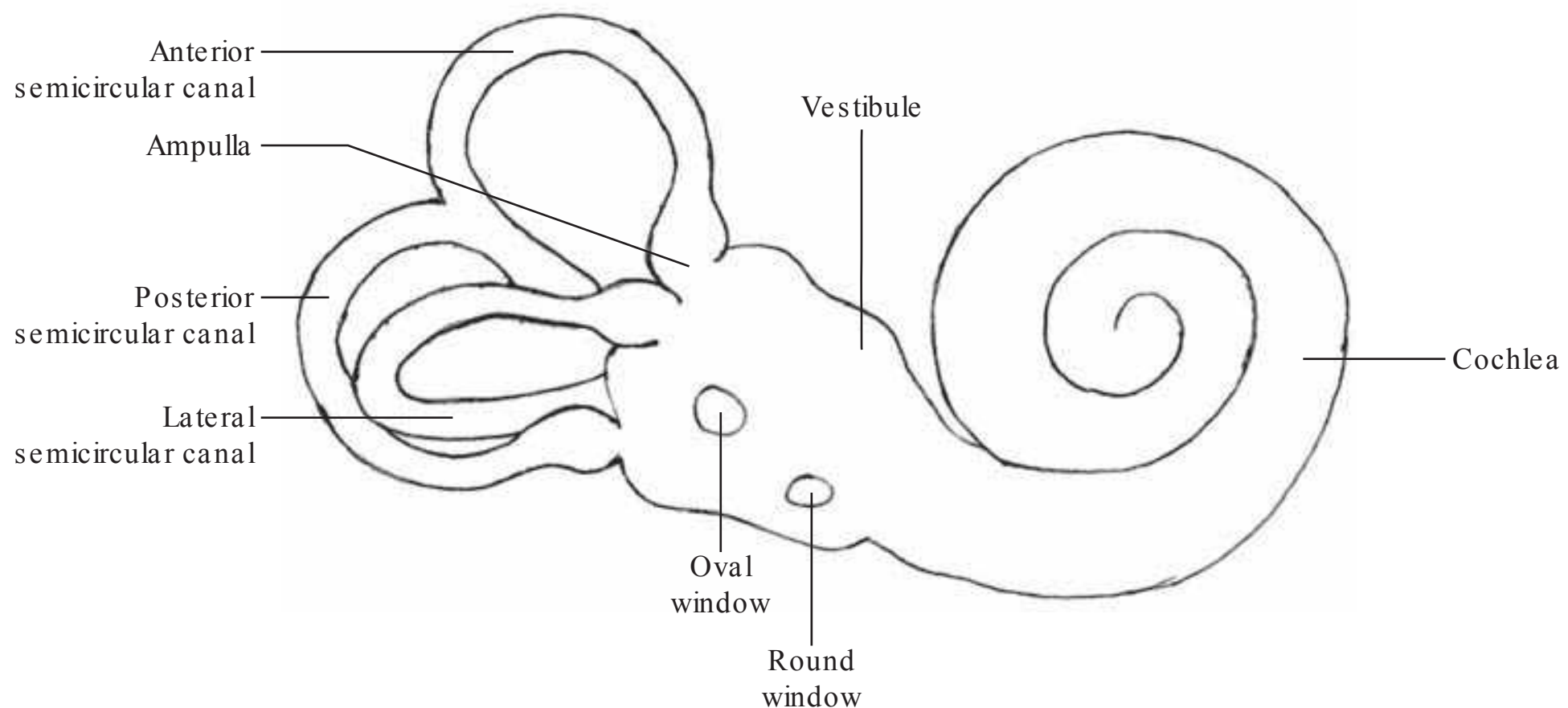
- The middle ear is a cavity (tympanic cavity) in the petrous part of the temporal bone (Fig. 23.10).
- It communicates anteriorly with the nasopharynx through the auditory tube (Fig. 23.10) and posteriorly with the mastoid air cells of the mastoid part of temporal bone. The auditory tube helps in equalisation of pressure in the middle ear and the pharynx.
- The medial wall of the middle ear separates the tympanic cavity from the inner ear, and it has two openings known as oval and round windows (described later)
- The tympanic cavity contains three ear ossicles—malleus, incus and stapes (Fig. 23.10)—and two small muscles—tensor tympani and stapedius. These muscles protect the inner ear from loud sounds by dampening the vibrations.
- The tympanic cavity is lined by simple cuboidal epithelium, which is continuous with the inner layer of the tympanic membrane.
- The epithelium in the auditory tube changes to pseudostratified epithelium with goblet cells near its pharyngeal opening.

## **INNER EAR**

- The inner ear is located in the petrous part of the temporal bone. It consists of bony labyrinth and membranous labyrinth.
- The bony labyrinth is a bony cavity. It contains a fluid-filled sac, the membranous labyrinth, and the fluid within the membranous labyrinth is known as endolymph.
- Between the walls of bony and membranous labyrinths is a space known as perilymphatic space. The fluid within this space is called perilymph.
- The bony labyrinth consists of the following parts: vestibule, cochlea and three semicircular canals (Fig. 23.11).
- The membranous labyrinth consists of cochlear duct, utricle, saccule and three semicircular ducts (Fig. 23.12).

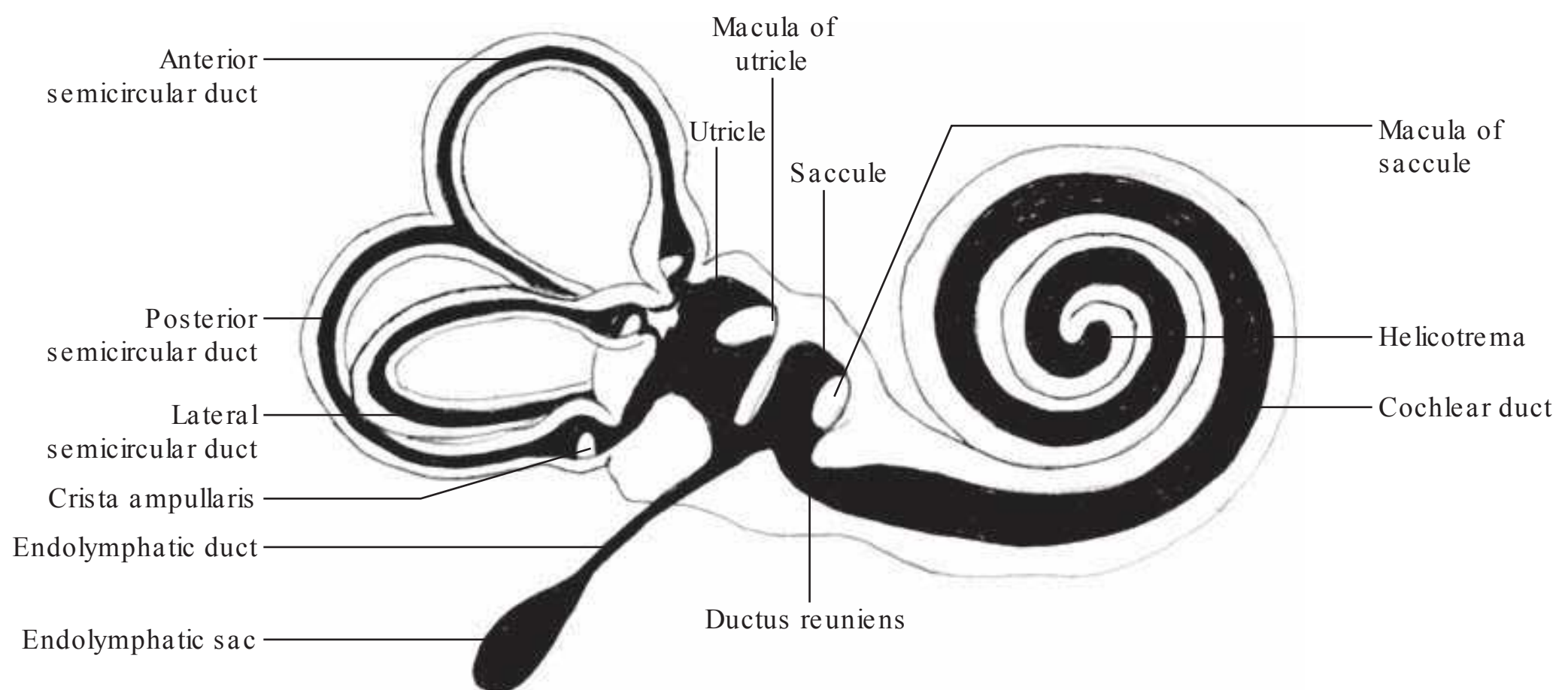
### **Vestibule**

- Vestibule is the central part of the bony labyrinth and lies between the cochlea and semicircular canals (Fig. 23.11).
- Anteriorly it communicates with cochlea, and posteriorly it has five openings for semicircular canals.



**Figure 23.11** Bony labyrinth.

- The lateral wall of the vestibule, which separates the vestibule from the middle ear, has two openings: fenestra vestibuli or oval window and fenestra cochleae or round window (Fig. 23.11). The oval window is closed by the base of stapes (Fig. 23.10) and the round window is closed by a membrane called secondary tympanic membrane.
- The medial wall has an opening known as aqueduct of vestibule; the endolymphatic duct (described later) is present in it.
- The parts of membranous labyrinth inside the vestibule are utricle and saccule (Fig. 23.12). The wall of both utricle and saccule consists of a thin sheet of fibrous connective tissue, covered with a single layer of squamous or cuboidal cells. Both utricle and saccule have a thickened area in their wall known as macula (Fig. 23.12). The macula contains the receptors for sensing the linear acceleration.



**Figure 23.12** Membranous labyrinth.

### *Endolymphatic Duct*

- Both utricle and saccule have a small duct, and these ducts unite and form the endolymphatic duct, in a Y-shaped manner (Fig. 23.12).
- The endolymphatic duct is present in the aqueduct of vestibule. The terminal expanded part of the duct is known as endolymphatic sac (Fig. 23.12).



## Semicircular Canals

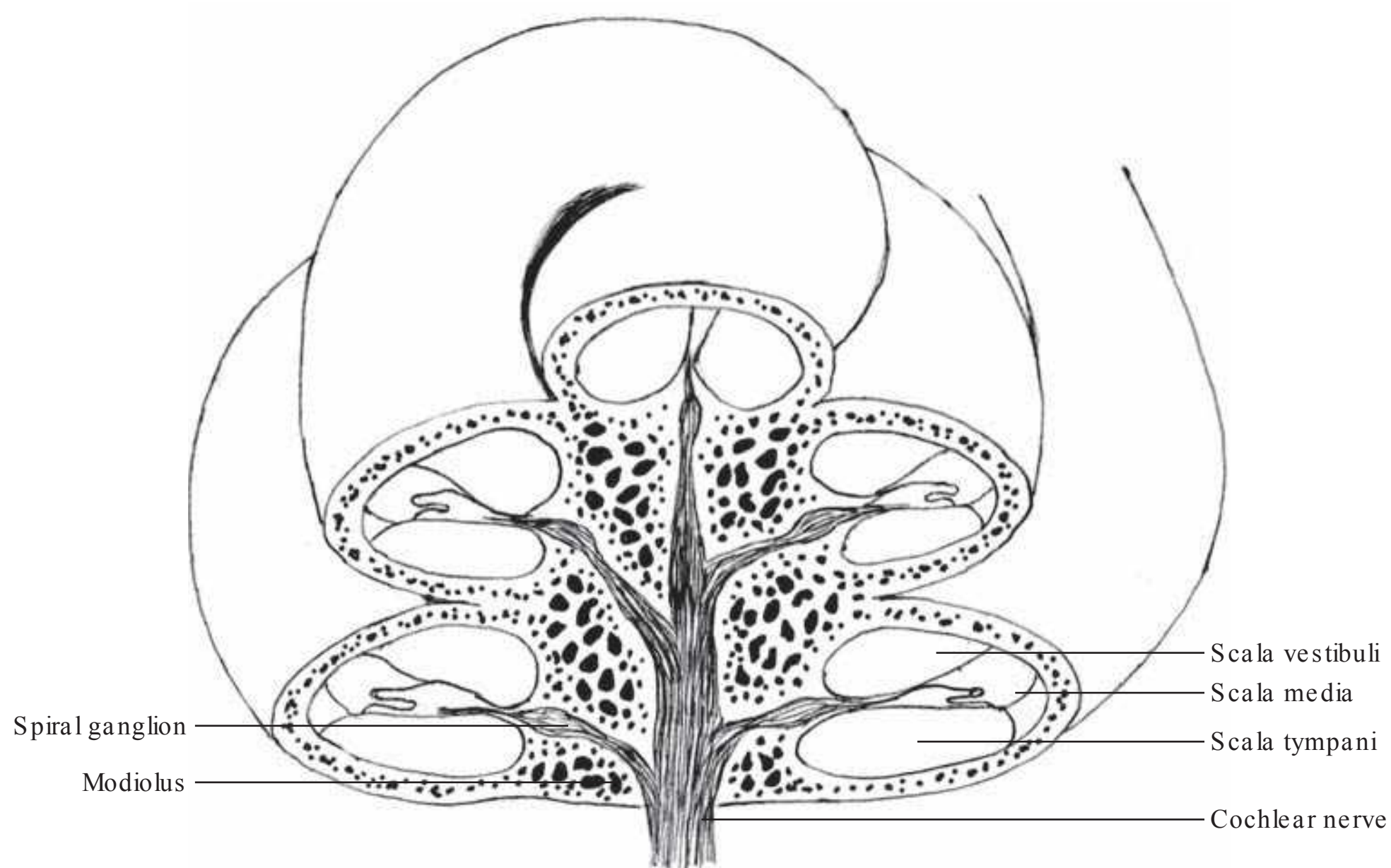
- There are three semicircular canals: anterior (or superior), posterior and lateral (Figs 23.10 and 23.11).
- The three semicircular canals are almost perpendicular to each other.
- Inside the semicircular canals, there are three corresponding semicircular ducts of the membranous labyrinth (Fig. 23.12).

### Semicircular Ducts

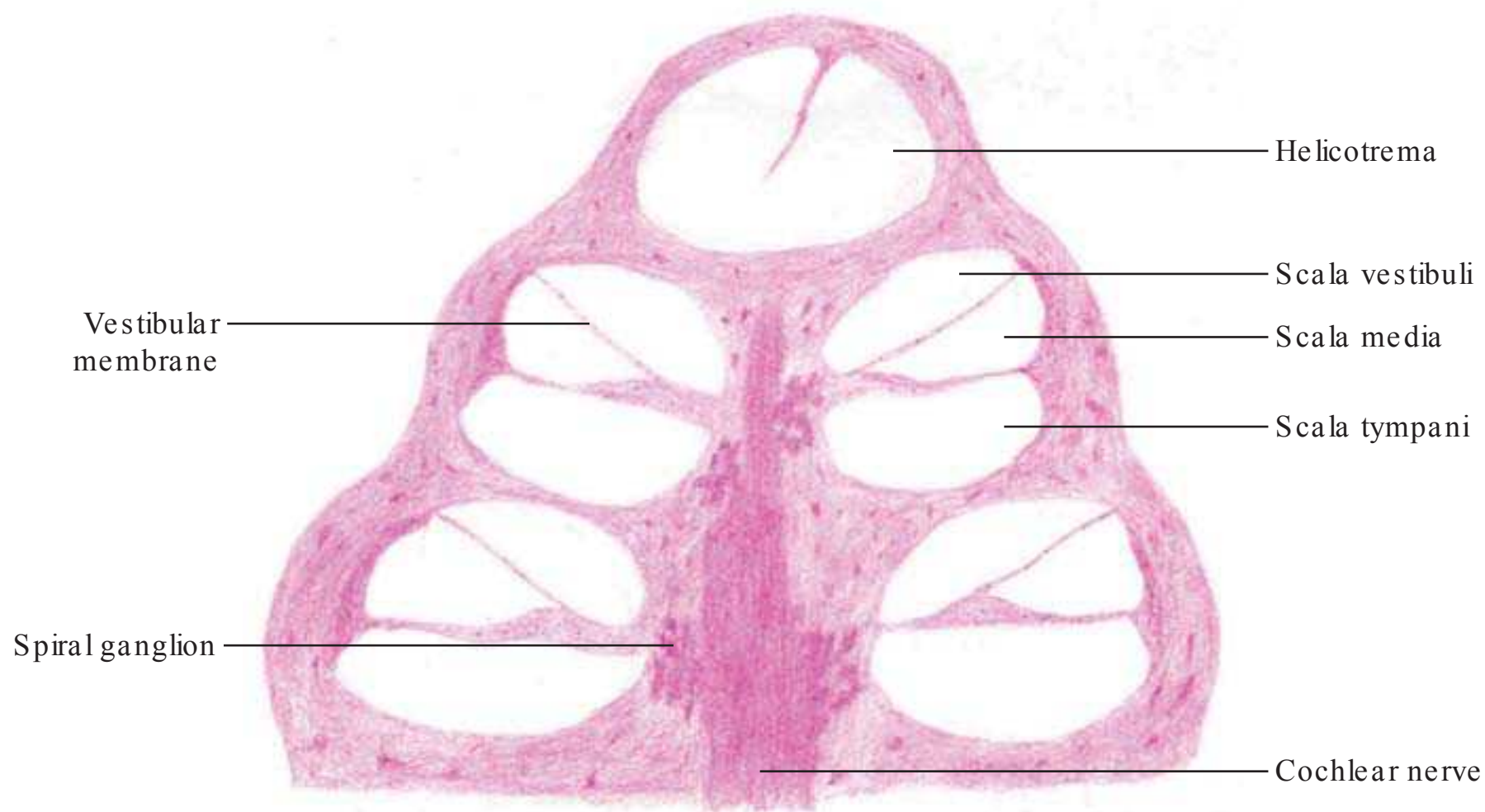
- As described earlier, there are three semicircular ducts inside the three corresponding canals. The anterior and posterior ducts are in vertical plane and the lateral duct is in horizontal plane. This kind of organisation helps in detecting the angular acceleration of the head in three different planes.
- Each duct has a dilated end, the ampulla, which opens into the utricle (Fig. 23.12).
- The three ducts open into the utricle through five openings, as one end each of the anterior and posterior canals fuse to form a common opening.
- Within each ampulla, there are elevated sensory areas known as cristae ampullares. It contains the receptors for sensing the angular acceleration.

## Cochlea

- Cochlea is a cone-shaped, spirally arranged canal (the cochlear canal) in the bony labyrinth, resembling the shell of a snail (Fig. 23.11).
- The canal spirals around a cone-shaped, bony, central axis known as modiolus (Figs 23.13 and 23.14). It takes two and one-half turns around the modiolus.

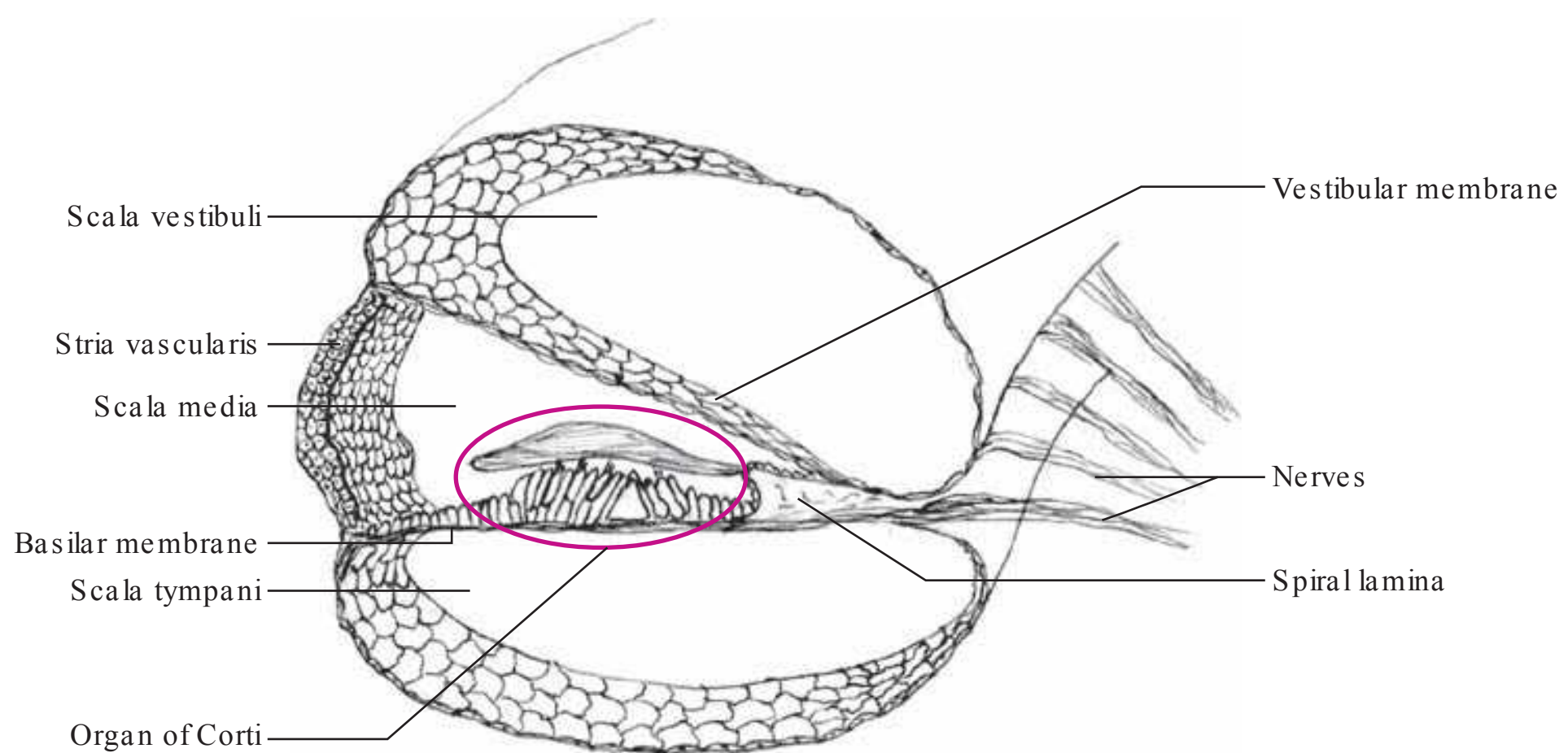


**Figure 23.13** Schematic diagram of a section of the cochlea.



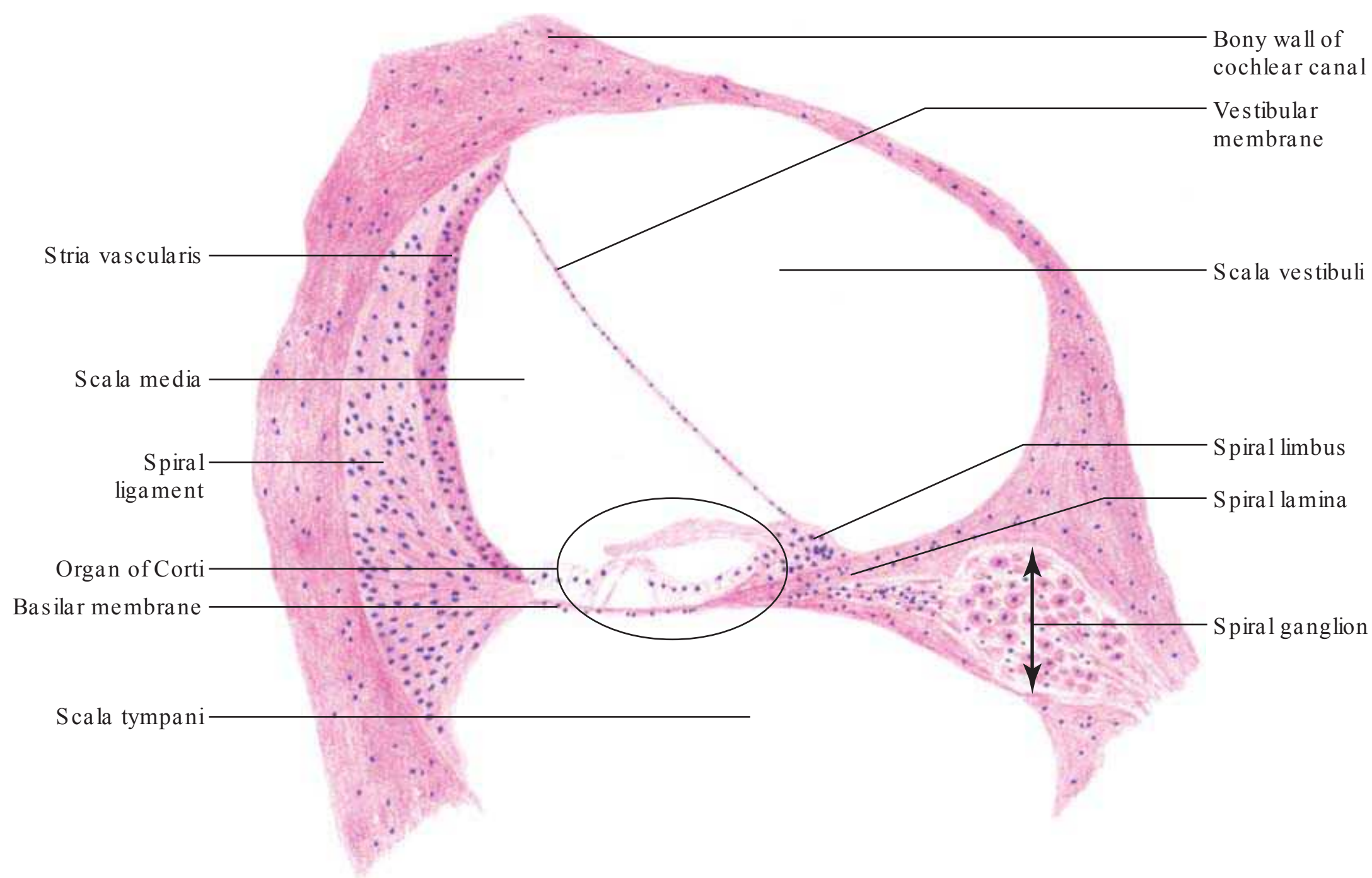
**Figure 23.14** Section of the cochlea in low magnification (H&E pencil drawing).

- The cochlear nerve emerges from the base of the cochlea (Figs 23.13 and 23.14).
- A bony shelf, known as spiral lamina, projects from the modiolus into the lumen of the cochlear canal (Figs 23.15 and 23.16). The spiral lamina does not reach the outer wall of the canal, and it extends only halfway across the width of the cochlear canal.
- The free edge of the spiral lamina is covered by connective tissue known as spiral limbus (Fig. 23.16).
- The part of membranous labyrinth inside the cochlea is the cochlear duct. It lies between the spiral lamina and the outer wall of the cochlear duct.
- The spiral lamina and the cochlear duct divide the cochlear canal into three compartments: scala vestibuli above, scala tympani below and scala media, which is the cochlear duct, in the middle (Figs 23.15 and 23.16).



**Figure 23.15** Schematic diagram of a section of the cochlear canal.





**Figure 23.16** Section of the cochlear canal in medium magnification (H&E pencil drawing).

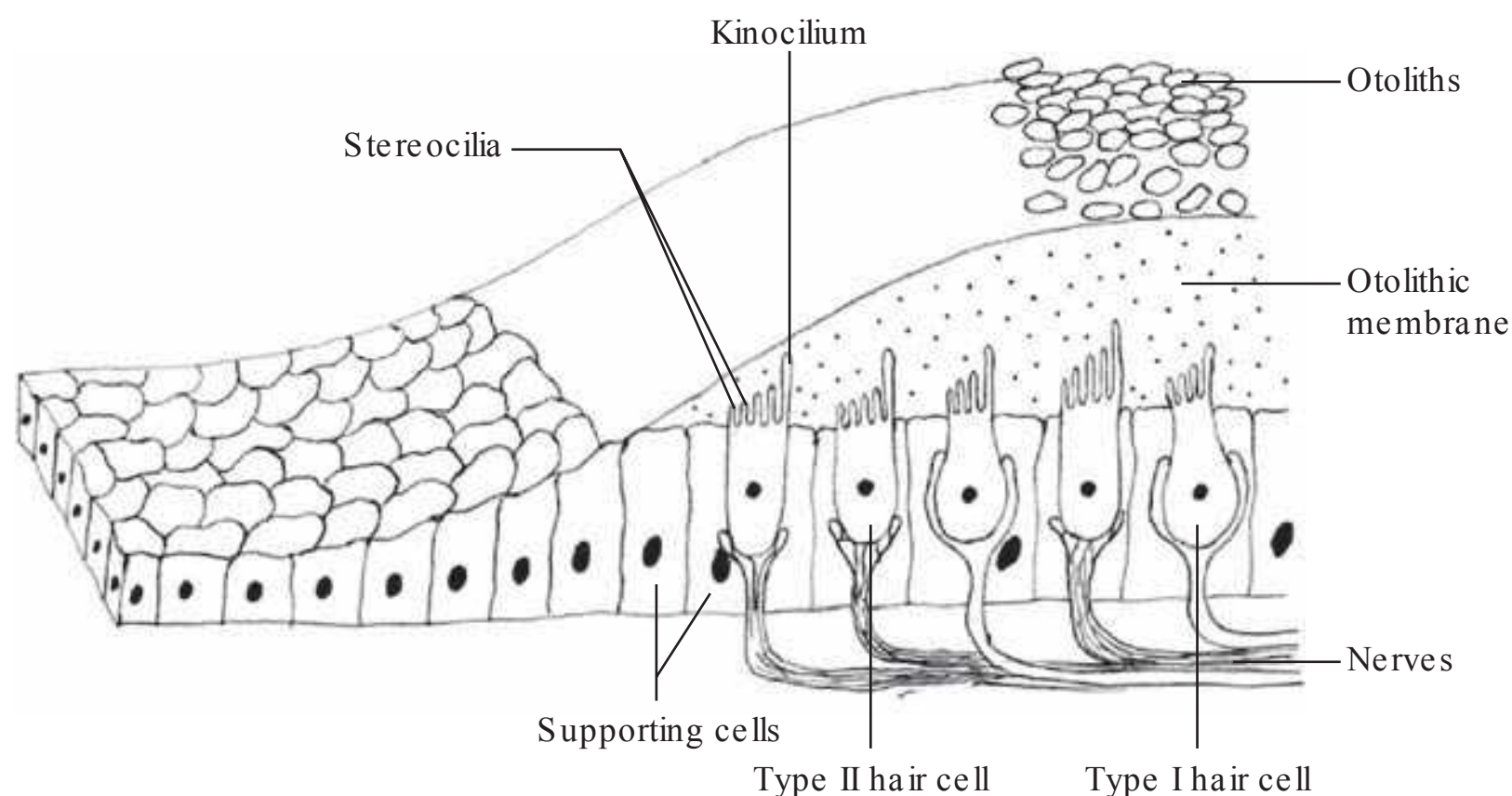
- The scala vestibuli and the scala tympani are filled with perilymph, and they communicate with each other at the apex of the cochlea through an opening called helicotrema (Fig. 23.14).
- At the base of the cochlea, the scala vestibuli is closed by the foot process of the stapes at the oval window and scala tympani is closed at the round window by the secondary tympanic membrane.
- The cochlear duct is filled with endolymph and houses the receptor for hearing, the organ of Corti.

#### *Cochlear Duct* (Figs 23.15 and 23.16)

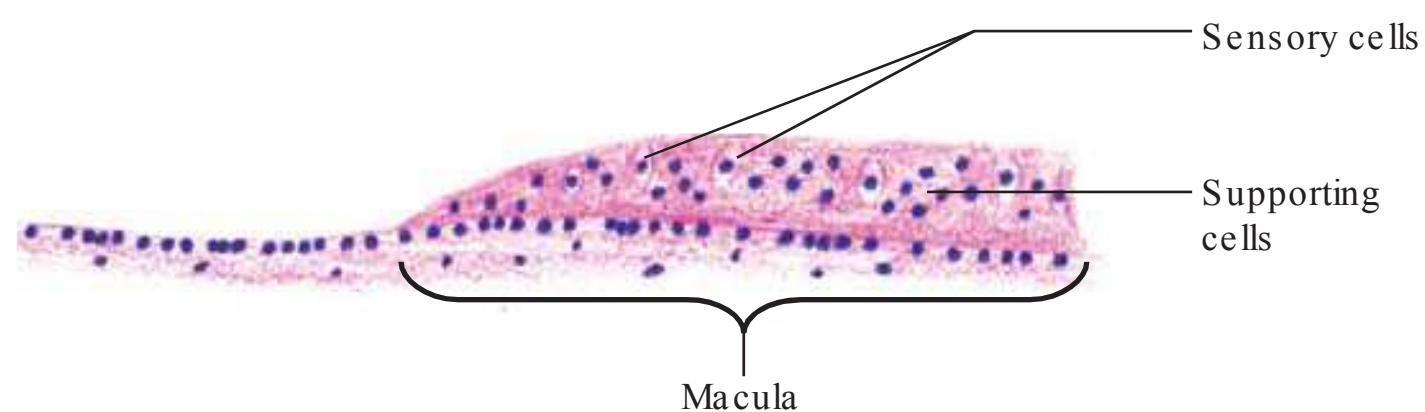
- The cochlear duct is a part of the membranous labyrinth inside the cochlear canal. Like the cochlear canal, it also undergoes two and one-half turns.
- It is connected to the saccule by a narrow duct known as ductus reuniens (Fig. 23.12). The opposite end of the duct ends blindly at the apex of the cochlea.
- It is separated from the scala vestibule by vestibular or Reissner's membrane. It extends from the spiral lamina to the lateral wall of the cochlear canal.
- The vestibular membrane consists of two layers of simple squamous epithelium separated by a basement membrane.
- The cochlear duct is separated from the scala tympani by spiral lamina and a fibrous sheet, the basilar membrane.
- The basilar membrane extends from the free edge of the spiral lamina to the spiral ligament.
- The spiral ligament is thickened endosteum of the outer wall of the cochlear canal (Fig. 23.16).
- The organ of Corti rests on the basilar membrane.
- In the lateral wall of the cochlear duct is a vascular area, the stria vascularis. It consists of stratified epithelium which is highly vascular.

### Receptor of Linear Acceleration: Macula (Figs 23.17 and 23.18)

- As described earlier, both utricle and saccule have a thickened area in their wall known as macula.
- The macula contains the receptors for sensing linear acceleration.
- The macula consists of two types of cells: sensory hair cells and supporting cells.
- Supporting cells are tall columnar cells with basal nuclei and have microvilli at the apex. These cells produce a gelatinous layer, the otolithic membrane, overlying the sensory cells. Crystals of calcium carbonate, known as otoliths or otoconia, overlie the otolithic membrane.
- Each hair cell at its free surface has numerous stereocilia arranged in a row and one cilium known as kinocilium. Both stereocilia and kinocilium are embedded in the otolithic membrane. The movement of stereocilia towards the kinocilium stimulates the hair cells.
- There are two types of hair cells: type I and type II. Type I hair cells are flask shaped and are surrounded by nerve endings. Type II hair cells are columnar in shape; the nerve endings are present at the base of these cells.



**Figure 23.17** Macula.

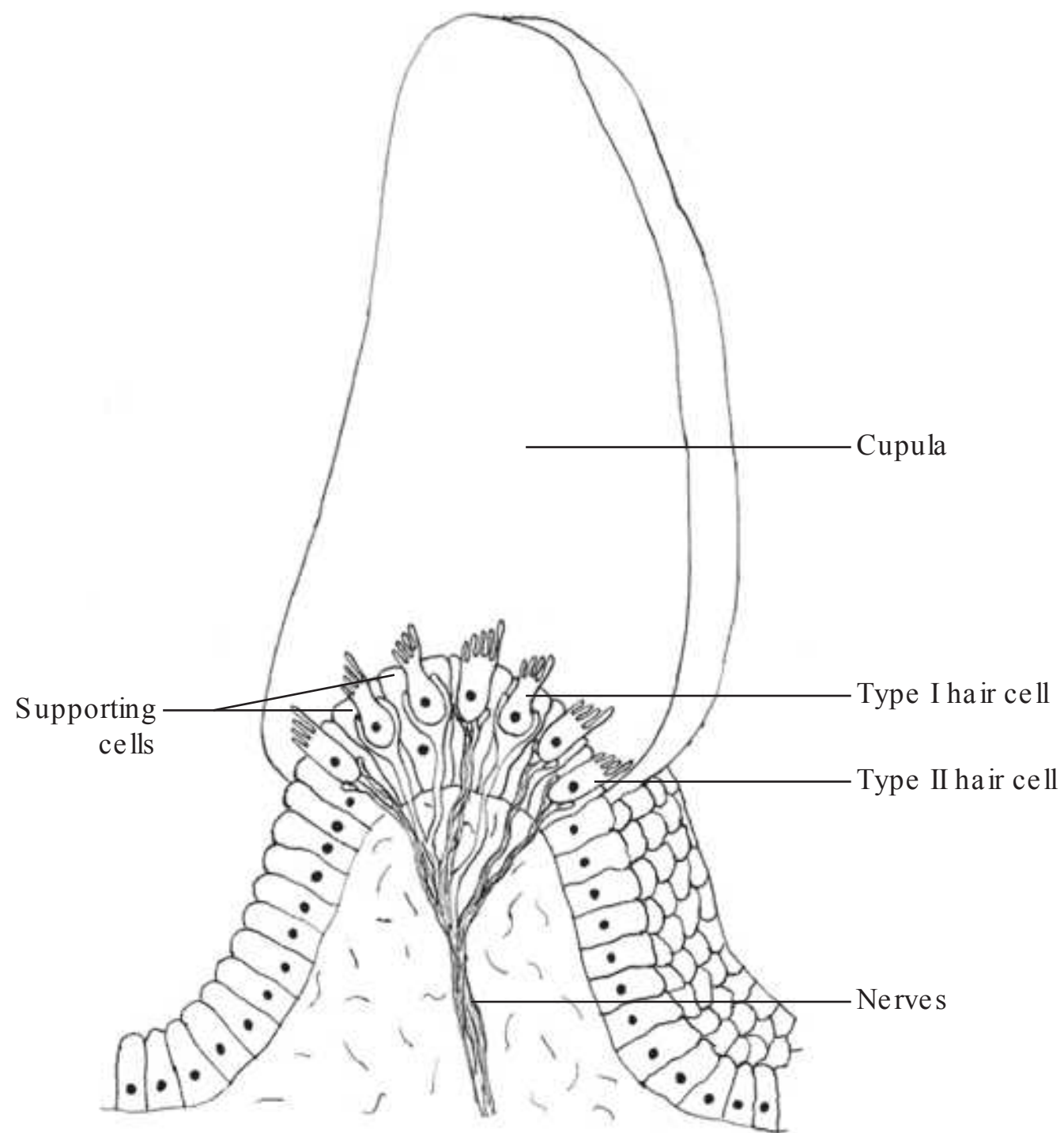


**Figure 23.18** Section of the macula in low magnification (H&E pencil drawing).

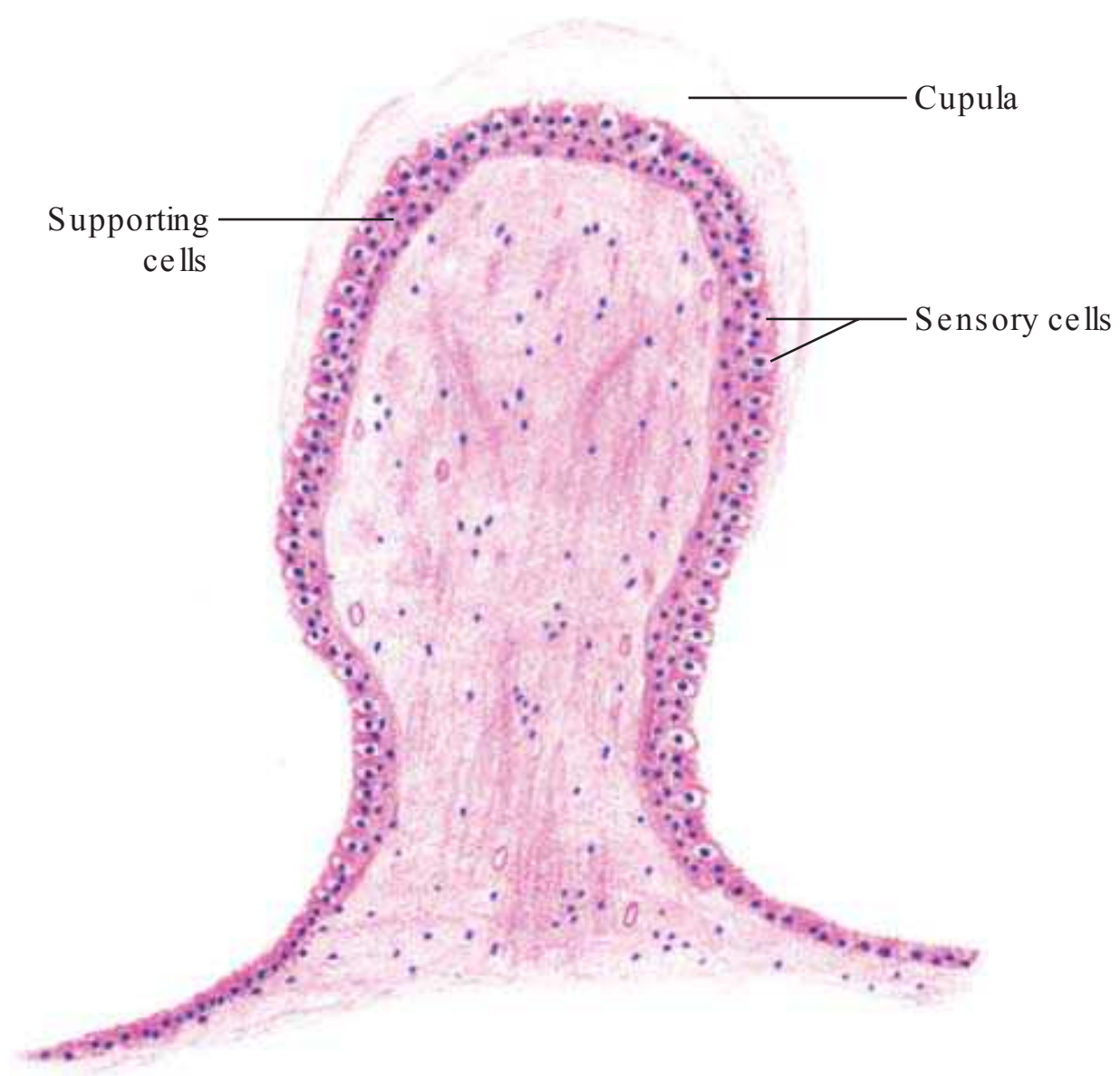
### Receptor of Angular Acceleration: Crista Ampullaris (Figs 23.19 and 23.20)

- As described earlier, within each ampulla there are elevated sensory areas known as cristae ampullares. It lies perpendicular to the long axis of the semicircular duct.
- Structurally, it is similar to the ampulla except that the gelatinous layer overlying the supporting and sensory cells is cone shaped, known as cupula; it does not contain otoliths.





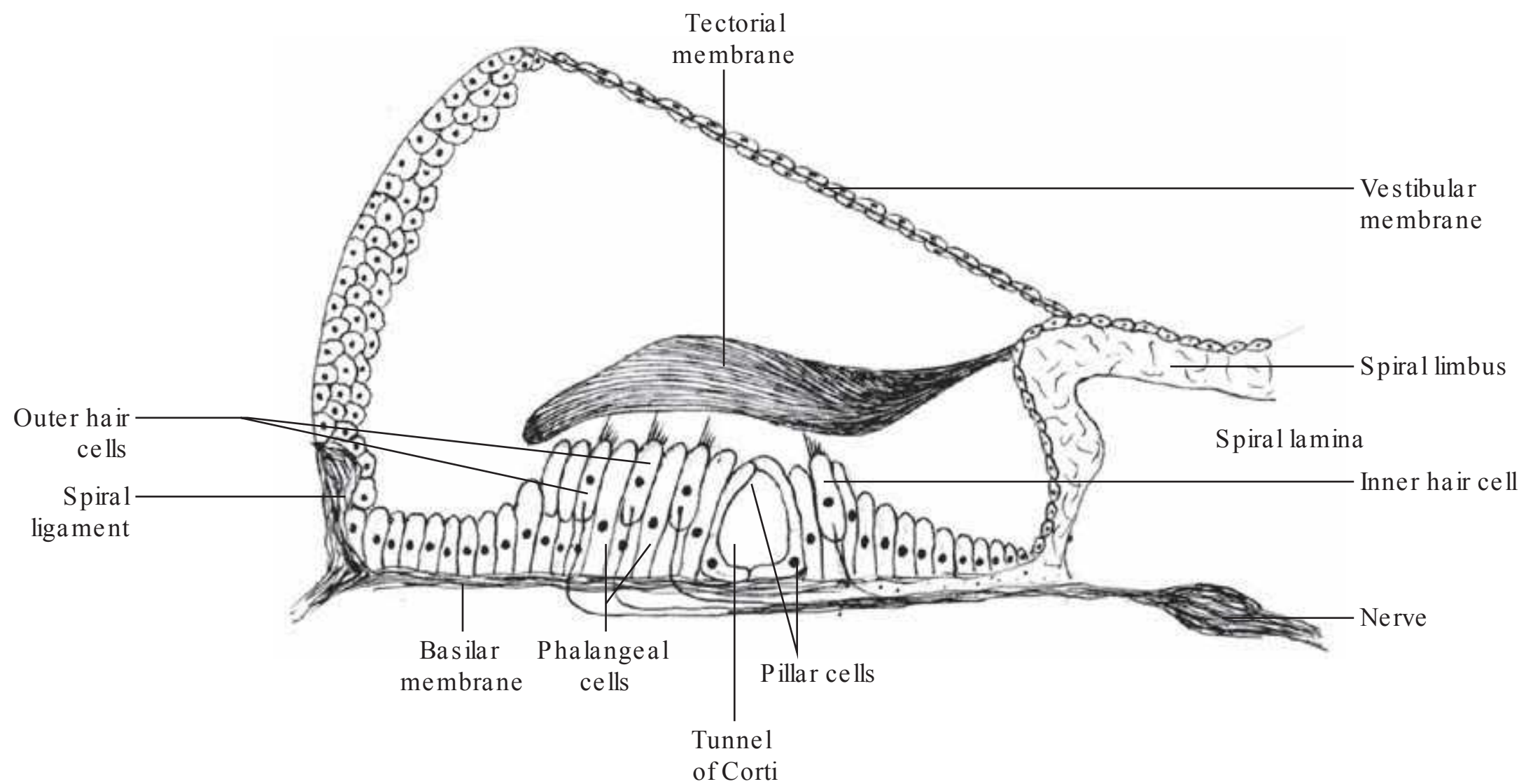
**Figure 23.19** Crista ampullaris.



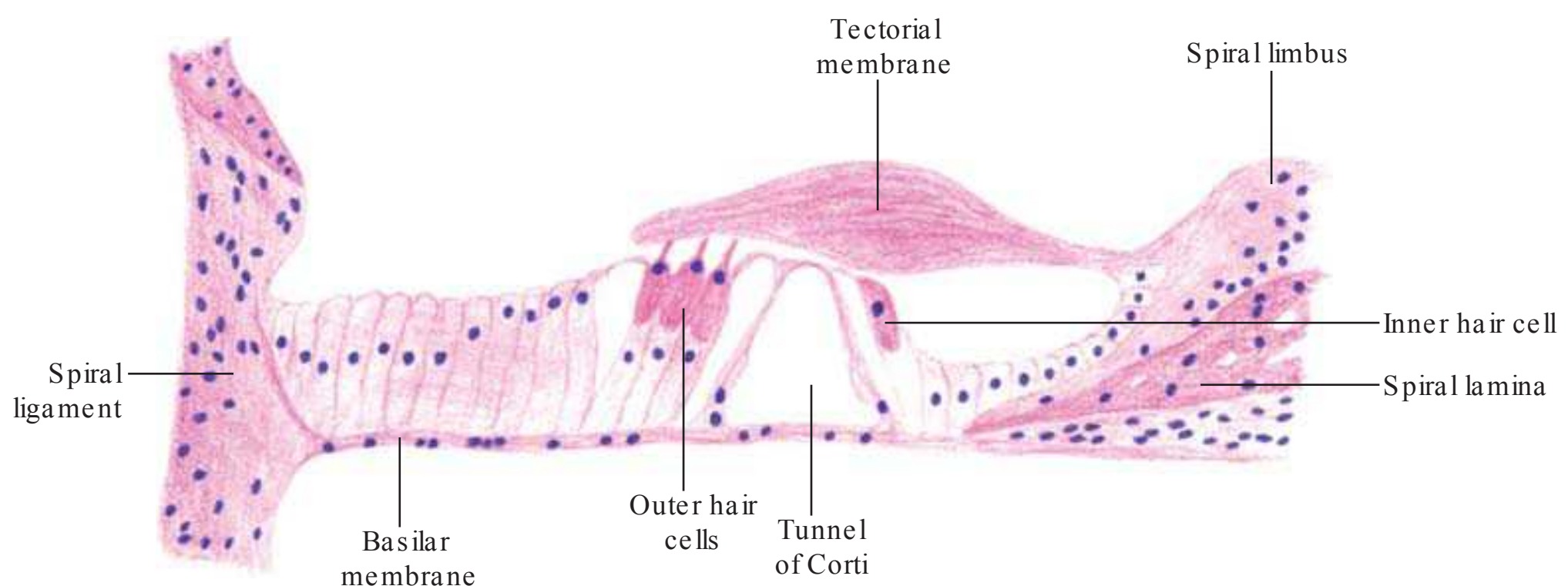
**Figure 23.20** Section of the crista ampullaris in low magnification (H&E pencil drawing).

### Receptor of Sound: the Organ of Corti (Figs 23.21 and 23.22)

- The organ of Corti is present in the scala media of the cochlea.
- It rests on the basilar membrane.



**Figure 23.21** Organ of Corti.



**Figure 23.22** Section of the organ of Corti in high magnification (H&E pencil drawing).

- It contains two types of receptors cells: inner and outer hair cells. The inner and outer hair cells are separated by the tunnel of Corti.
- The stereocilia of the outer hair cells are in contact with a filamentous sheet, the tectorial membrane. The tectorial membrane is supported by the spiral limbus.
- The dendrites of bipolar cells synapse with the hair cells. The cell bodies of the bipolar cells are located in the spiral ganglia in the modiolus (Figs 23.13 and 23.16). The axons of the bipolar cells form the cochlear nerve which passes through the modiolus.
- There are two types of supporting cells in the organ of Corti: the pillar cells support the tunnel of Corti and the phalangeal cells support the hair cells.

## HEARING

- Sound waves are received by the external ear from the external environment.
- These sound waves vibrate the tympanic membrane.
- From the tympanic membrane, sound waves are transmitted to the oval window through the ear ossicles.



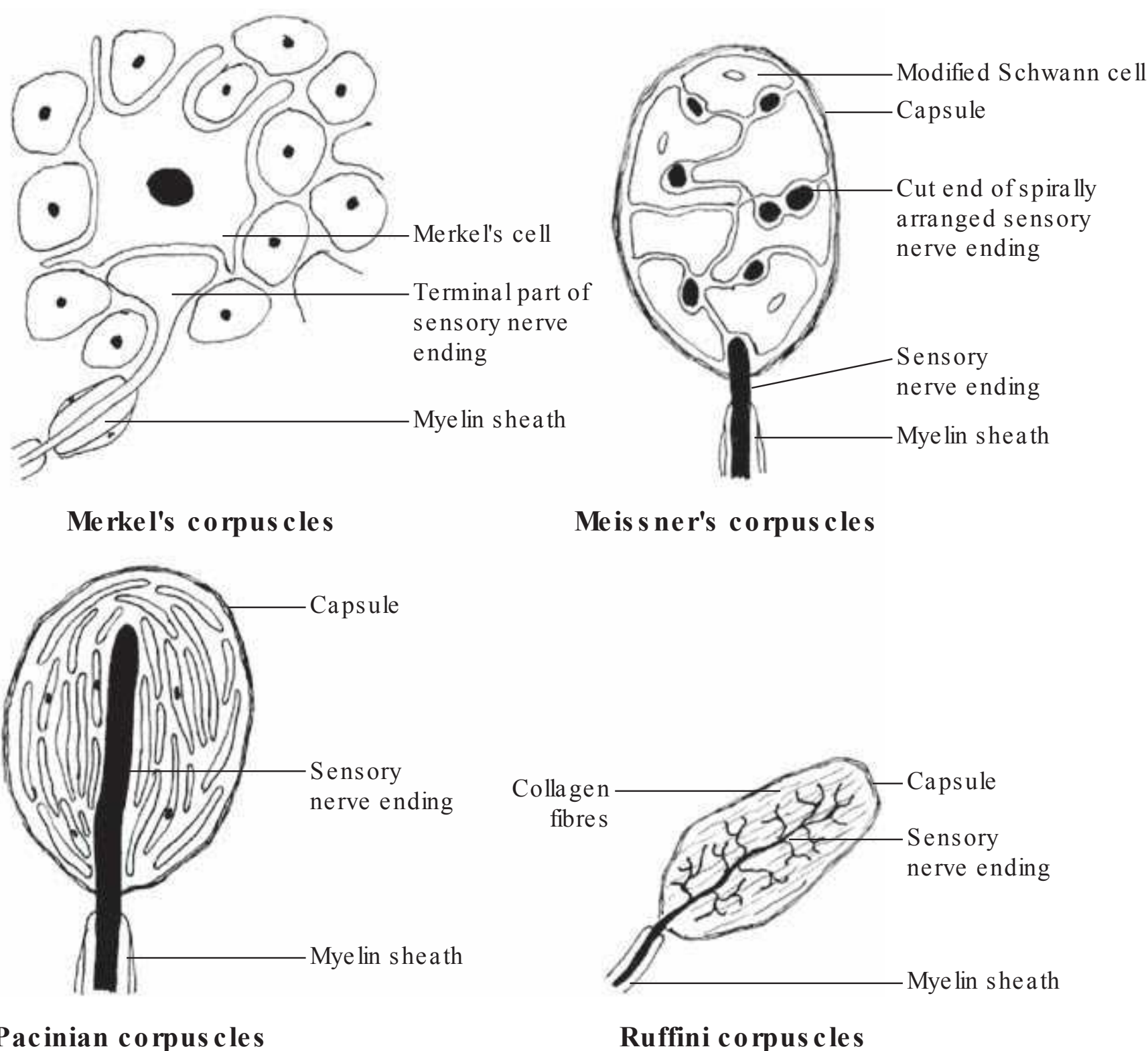
- The outer and middle ears amplify the vibrations produced by sound waves. The large pinna transfers the vibration to the smaller tympanic membrane, which is much larger than that of the foot plate of stapes. The ear ossicles function as a lever to intensify the vibrations.
- Vibrations of the foot plate of the stapes are transferred to the perilymph in the vestibule and subsequently in the scala vestibule and scala tympani.
- Through the vestibular membrane, the vibrations reach the endolymph of scala media.
- Vibration in the basilar and tectorial membranes produces movement in the stereocilia of hair cells, and nerve impulse is generated.

## CUTANEOUS RECEPTORS

- Various cutaneous receptors are present in the skin; hence skin is considered as a sensory organ.
- Cutaneous receptors are the terminal branches of a sensory neuron; they respond to pain, touch, pressure and temperature.
- Different types of cutaneous receptors are described in the following text.

### MERKEL'S CORPUSCLES

- Merkel's corpuscles are the touch receptors present at the base of the epidermis.
- They are nerve endings associated with Merkel's cells (described in Chapter 22). The nerve ending lacks Schwann cells, and its terminal part expands into a disc-shaped ending (Fig. 23.23).
- They are seen in the thick skin of palms and soles.



**Figure 23.23** Cutaneous receptors.

### MEISSNER'S CORPUSCLES

- Meissner's corpuscles are touch and pressure receptors.
- They are encapsulated endings. The sensory nerve endings are covered by several layers of modified Schwann cells (Fig. 23.23).
- Inside the capsule, the nerve endings lack myelin sheath and it is arranged spirally.
- These receptors are located in the dermal papillae of the skin, underneath the basement membrane of epidermis in palmar and plantar skin.

### PACINIAN CORPUSCLES

- Pacinian corpuscles are pressure receptors located in the deeper part of the dermis, hypodermis and periosteum.
- They are ovoid structures, and each corpuscle has a nerve ending covered by capsules (Fig. 23.23; also see PMG 22.3, page 334).
- A myelinated sensory nerve fibre enters the capsule and loses its myelin sheath.
- The capsule consists of concentric layers of flat cells, and the spaces between the layers are filled with tissue fluid.

### RUFFINI CORPUSCLES

- These receptors have numerous fine branches from a myelinated axon, which loses its myelin.
- Branches of the myelinated axons are surrounded by collagen fibres and a capsule of connective tissue (Fig. 23.23).
- They are present in deep dermis.

## CLINICAL CORRELATES

### Corneal Transplantation

- Since the corneal stroma lacks blood vessels, there is no immunological reaction after corneal transplantation, and this results in a high success rate of corneal transplantation.

### Retinal Detachment

- It is the separation of the pigment layer from the nervous layer of the retina. It is of two types: non-rhegmatogenous, in which the two layers get separated without retinal tear, and rhegmatogenous, in which there is retinal tear.

### Eyelid

- Inflammation of the eyelid is known as blepharitis. An external styne is an infection of the sebaceous glands of Zeis or an infection of the apocrine sweat glands of Moll at the base of the eyelashes. It is a self-limiting disease and resolves in 8–10 days without treatment.

### Cataract

- Lens is a transparent structure; development of opacity in the lens is known as cataract.

## KEYPOINTS

### Cornea (Fig. 23.2; PMG 23.1)

- It consists of the following five layers (from anterior to posterior):
  - (a) Anterior epithelium
  - (b) Bowman's membrane (anterior limiting lamina)



- (c) Substantia propria (stroma)
- (d) Descemet's membrane (posterior limiting membrane)
- (e) Posterior epithelium (corneal endothelium)

**Retina** (Fig. 23.3; PMG 23.2)

- It consists of the following 10 layers (from outside inwards):
  - (a) Pigment cell layer: It is a single layer of cuboidal cells resting on a thick basement membrane (Bruch's membrane). These cells contain melanin granules.
  - (b) Layer of rods and cones: These are the photoreceptors; they pass through the external limiting membrane.
  - (c) External limiting membrane: It is formed by Muller cells.
  - (d) Outer nuclear layer: This layer consists of nuclei of photoreceptors.
  - (e) Outer plexiform layer: In this layer, axons of rods and cones synapse with the dendrites of bipolar cells.
  - (f) Inner nuclear layer: It contains nuclei of bipolar cells, Muller cells, horizontal cells and amacrine cells.
  - (g) Inner plexiform layer: In this layer, the axons of bipolar cells synapse with the dendrites of ganglion cells.
  - (h) Ganglionic cell layer: This layer consists of cell bodies of ganglion cells.
  - (i) Nerve fibre layer: Axons of the ganglion cells travel in this layer towards the optic disc.
  - (j) Inner limiting membrane: This layer consists of the processes of Muller cells.

**Eyelid**

- From the anterior to posterior surface, the eyelid consists of four layers:
  - (a) Skin
  - (b) Muscle layer
  - (c) Tarsal plate
  - (d) Conjunctiva

**Glands in Eyelid**

Glands	Location
Glands of Moll (modified apocrine sweat glands)	Associated with eyelash
Glands of Zeis (sebaceous glands)	Associated with eyelash
Meibomian glands (sebaceous glands)	In tarsal plate

**SELF-ASSESSMENT**

1. Enumerate the layers of cornea. Briefly describe the composition of each layer.
2. Enumerate the layers of retina. What are the different types of cells in the neural layer?
3. Name the different types of glands present in the eyelid.
4. What is the lining epithelium of conjunctiva?
5. What are the different types of hair cells present in the cristae ampullares?
6. Describe the structure of the organ of Corti.

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